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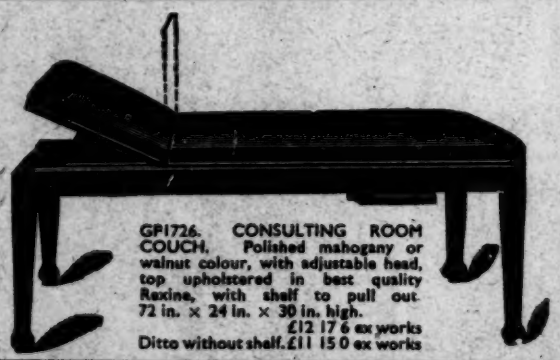

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BRITISH MEDICAL JOURNAL

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THE DEFINITION AND ASSESSMENT OF RESPIRATORY FUNCTION*

BY

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PART I

Many clinicians who specialize in diseases of the lungs will declare quite honestly that they understand little if anything about lung function. There are good reasons for this. The constant presentation of special tests, some simple and some very complicated, dealing with one particular aspect of lung function, as a general clinical test of great value has made the clinician justifiably sceptical. The great gap between modern knowledge of respiratory function and what is taught to the students in their most receptive years is unfortunate. In the hurly-burly of respiratory research few pause to consider and agree upon what gains have been made and what may be of real practical value. On the other hand, it is surprising that chest physicians and surgeons, who spend many years perfecting their skill and increasing their knowledge, are reluctant to devote a year or so to the study of respiratory physiology. Without such a training in early professional life it is hardly possible to develop an informed curiosity concerning the problems of respiratory function.

The new era of thoracic surgery has come as an abrupt challenge in this field. Lung resection and collapse can be life-saving measures, but there is always the problem of whether the remaining lung will support a tolerable existence. Operations are frequently contemplated on a background of disease, and thus, although the lung that will remain may have impaired function, some attempt must be made to assess this function so that the feasibility and safety of the operation can be reasonably foretold.

The function of the lungs is to maintain normal and nearly constant oxygen and carbon dioxide tensions and content in the arterial blood in all physiological circumstances, without causing any undue sensation of ventilatory discomfort or adverse effect on the heart or any other organ. This constancy of the arterial blood gases in all degrees of activity and oxygen usage is maintained only by the efficient transfer of gas between the alveolar air and the blood passing through the alveolar capillaries. Such a transfer demands the intimate bringing together of blood and gas and the maintenance of an adequate gas-tension gradient between them. It is the function of ventilation that maintains and freshens the alveolar gases despite the constant interchange of oxygen and carbon dioxide with the venous blood. This ventilation must not only be adequate in total quantity but must be efficiently distributed to all alveoli through which blood is flowing. Similarly, the venous blood from the right heart must be efficiently distributed to all ventilated alveoli. In this way an enormous blood–gas interface is created. Any lack of correlation between the ventilation and circulation of the lungs, in the form of ventilation of unperfused alveoli or perfusion of underventilated alveoli, will mean wasted ventilatory effort or imperfect oxygenation of blood, and will cause a reduction in the effective blood–gas interface. Finally, there must be no undue interference with the diffusion of gases through the structures present between the alveolar gases and the blood.

*Adapted from lectures given in the "Science and Medicine" series, Postgraduate Federation (London University), 1950–1.

VENTILATION

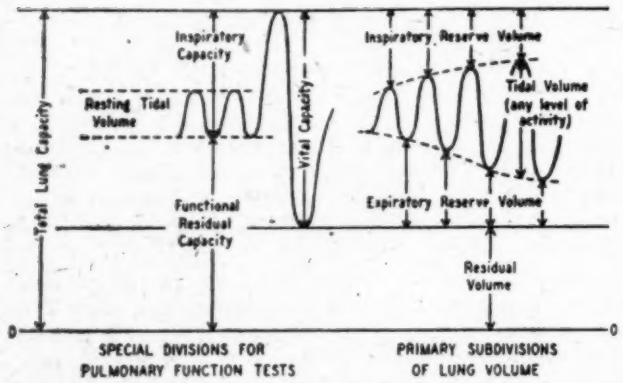
The purpose of lung ventilation is to refresh the lung alveoli constantly with atmospheric air so that adequate oxygen diffuses into, and carbon dioxide diffuses from, the blood as it passes through them. The act of ventilation is unconscious, and, although a healthy person may be transiently aware of his respiration, it causes him no discomfort or embarrassment. The only important factor causing changes in the volumes ventilated in everyday life is the degree of body activity. If normal subjects exercise very violently, or subjects with lung disease increase their activity unduly, then they will complain of "shortness of breath" or dyspnoea. In the past this sensation has been attributed to many factors such as excess carbon dioxide, anoxaemia, and increased hydrogen-ion concentration, and their effect upon the central nervous system. In recent years increasing evidence has accumulated that dyspnoea is no more than ventilatory discomfort, when the volumes ventilated are excessive for the ventilatory capacity present. Dyspnoea can thus be caused by very large ventilatory volumes in the presence of a normal ventilatory capacity, or by very moderate ventilatory volumes in the presence of a severely impaired ventilatory capacity.

Lung Volumes

The lung volumes—the boundaries, as it were, within which ventilation takes place—have for many years been regarded as one of the most important quantitative measurements in the assessment of lung function. There

is no doubt that undue emphasis has been laid upon this aspect. The study of lung volumes alone in various lung diseases can be particularly misleading if the observers assume that changes in the lung volumes are closely correlated with total lung function or the severity of a particular disease.

The terminology employed in the study of lung volumes has been so diverse that unnecessary confusion has arisen. Christie (1932) made excellent suggestions to standardize the nomenclature, and his terminology has been almost universally accepted. Recently, however, a further standardization has been put forward by a large group of interested workers (Pappenheimer *et al.*, 1950), and their suggestions are a further advance (see Diagram). The primary subdivisions of lung volume are



Subdivisions of the lung volume (after Pappenheimer *et al.*, 1950). All gas volumes corrected to body temperature, pressure, and saturated with water vapour (B.T.P.S.).

shown on the right, and apply to all levels of respiratory effort and contain no overlapping volumes. On the left are the terms used when the patient is studied at rest. It will be noted that the expression "air" to denote a volume is carefully avoided. All gas volumes should be corrected and stated at body temperature, pressure, and saturated with water vapour (B.T.P.S.), as the vital phenomena occur within the chest and not within the spirometer.

The vital capacity is, by Hutchinson's (1846) original definition, the volume of gas that can be expelled by a maximal expiration following a maximal inspiration. It can be measured by expiring into any gas-volume-measuring apparatus that affords no appreciable resistance and is of sufficient accuracy. In the closed circuits usually employed, when a tracing is obtained, high percentages of oxygen are used. Accurate volumetric tracings while breathing air or any other mixtures of gases can be obtained by the box-bag technique (Donald and Christie, 1949). In a series of observations on four normal subjects by this method I could find no significant change in vital capacity when breathing oxygen, air, 12% oxygen and nitrogen, or 5% carbon dioxide in air. When determining the vital capacity several trials are carried out. If successive measurements show a large increase, owing to better understanding and effort, then the procedure should be continued until nearly constant values are obtained. According to definition, the maximal value observed is recorded as the vital capacity.

If a respiratory tracing is taken over a period the two components of the vital capacity, the inspiratory capacity (O.T. complemental air) and the expiratory reserve volume (O.T. reserve air) can also be determined. This subdivision affords some difficulty even in normal subjects. There is a tendency to alter and vary the "respiratory level" (which can be precisely described by the volume of air in the chest at the end of quiet expiration) during such breathing gymnastics. Further, subjects with respiratory disability are even more prone to such alterations. The temporary increase of oxygen uptake resulting from a deep inspiration (Armitage and Arnott, 1949) also makes the analysis of the record more difficult.

The vital capacity alone is not of great value in assessing respiratory disability. A patient with greatly reduced vital capacities may have remarkably good ventilatory function, and vice versa. The two subdivisions of vital capacity have also been overinterpreted.

It was thought that the determination of the residual volume (that volume of gas remaining in the lungs after a maximal expiration) by various indirect methods would give far more meaning to lung-volume measurements, particularly as this would allow the total lung capacity to be studied. Thus the residual volume and the total capacity would give the minimal and maximal lung volumes. The residual volume could be considered not only absolutely but also as a percentage of the total lung volume. Christie (1932) has reviewed 47 methods of determining the residual volume.

Open-circuit Method.—The so-called "open-circuit" of Darling *et al.* (1940) is used extensively in America. When a subject breathes oxygen the total amount of nitrogen in the expired gas will be a simple function of the volume of gas in the lungs and the change in the lung nitrogen concentration. The expired gas is collected in a large spirometer (Tissot) for seven minutes. The patient is then switched out of the oxygen circuit and told to exhale maximally, an alveolar sample being taken with an evacuated gas-sampling tube. There are many valid criticisms of this method: poor washing-out of underventilated areas of lung, no tracing is available, and direct alveolar samples (end of maximal expiration) are unreliable in many lung diseases.

Closed-circuit Method.—This method of determining the residual volumes, which is used extensively in this country and Europe, employs a closed circuit and a physiologically inactive gas. Its principle is that the degree of dilution of a known quantity of inert gas is a simple function of the combined volumes of the lungs and the spirometer circuit. In 1800 Humphry Davy used hydrogen for this purpose. Van Slyke and Binger (1923) measured the residual volume by first determining the functional residual capacity during quiet normal breathing. Christie (1932) improved this technique and used the nitrogen present in the lungs at the time of turning the patient into the circuit as his indicator gas. Herrald and McMichael (1939) introduced the important modification of running oxygen into the circuit so as to keep the spirometer tracing level. This procedure ensured a constant spirometric and circuit volume despite oxygen uptake. They also employed a katharometer, which, by measuring the changing thermal conductivity of the gas, indicated the completion of mixing in the circuit and lungs. McMichael (1939), by reintroducing hydrogen as the indicator gas, with its high thermal conductivity, was able to use the katharometer not only to determine the rate and completion of mixing, but also the final concentration of hydrogen. Meneely and Kaltreider (1941) introduced the use of helium as the indicator gas. It has all the advantages of hydrogen without the risk of explosion, and it has been almost universally adopted for this purpose. These workers also pointed out that the rate of mixing of helium in the lungs, while measuring the residual air, was greatly retarded in emphysema.

The present methods of determining lung volumes are undoubtedly satisfactory, and the results obtained are certainly not far from the actual volumes being measured. Lung-volume studies of the same patients by the open- and closed-circuit methods have shown a remarkable agreement despite the faults of the simpler method (Gilson and Hugh-Jones, 1949). Many excellent studies of the lung volumes in various types of pulmonary disease are available. The stage has now been reached where it is more important to consider the value and meaning of lung-volume determinations than to attempt to improve their accuracy. It is also important that the values and ranges of variation of the lung volumes in normal persons at various ages should be more carefully determined.

The upper "normal" limit of the residual volume of the lungs, when expressed as a percentage of the total capacity, is usually considered to be from 20 to 30%, increasing slightly with age. However, in recent years more and more instances have been reported of healthy persons, particularly those over 50 years of age without any history of lung

disease or dyspnoea, with a residual volume of well over 40% of their total lung capacity (Greifenstein *et al.*, 1952). This is in no way surprising to anyone who has attempted to measure biological phenomena, but it has not deterred an appreciable number of workers from assessing the degree of severity of such diseases as pulmonary emphysema by this figure alone.

Pulmonary Emphysema

The old clinical observations that the lungs cannot empty adequately and that the respiratory level is much raised in this disease are in general confirmed. Stating this in terms of lung volumes, the residual volume and functional residual capacity are increased. However, the relationship of this increase to the degree of disability is very variable indeed. Baldwin *et al.* (1949b), in their extensive study of emphysema, divided the patients into four different groups, the severity of the disease being judged by the degree of arterial blood desaturation at rest and with exercise, by the presence or absence of carbon dioxide retention, and, finally, by the development of right heart failure. Although they found that most of these patients had a pronounced increase of residual volume (both absolutely and in relation to total capacity) the mean figure of the residual volume percentage of total capacity was in the region of 50 in all groups, despite the fact that these groups represented from moderate to very severe emphysema. Further, some of the most disabled patients had almost normal residual-volume/total-capacity ratios, and some patients in the earliest group, who did not even show arterial blood desaturation on brisk exercise, had some of the highest residual volumes. It has been my own experience and that of many other workers that, although the residual volume is usually greatly raised in emphysema, the relation of this rise to respiratory function, as judged by exercise tolerance and other tests, is most variable and unreliable.

Baldwin *et al.* also found, as many others have reported since, that there was very poor correlation between the vital capacity and ventilatory capacity (as measured by voluntary hyperventilation). Further, although the total capacity is increased in some cases of emphysema, this is by no means invariable, and most patients with this disease have a total capacity within the normal range. It follows, speaking generally, that if the total capacity, which is the combined residual volume and vital capacity, is not greatly altered in this disease then the size of the residual volume cannot be expected to correlate any better with function than the vital capacity.

Pulmonary Fibrosis

In diseases in which there is generalized pulmonary fibrosis the interpretation of lung volume data becomes even more difficult. Pulmonary fibrosis can occur without any significant degree of emphysema. In most of these patients all the various subdivisions of the total capacity are reduced proportionately and both the vital capacity and the residual volume are abnormally small.

However, if the vital capacity is reduced but the residual volume is still normal then the latter will represent an abnormally large percentage of total capacity. In the absence of knowledge of how pulmonary fibrosis may affect the filling and emptying of the lungs it is difficult, if not impossible, to assess the degree of emphysema in such patients on this evidence alone. The diagnosis of emphysema in pulmonary fibrosis is of great importance, as it is most desirable to be able to assess in what ways pulmonary fibrosis causes respiratory disability, apart from concomitant or secondary emphysema. Increase of the absolute residual volume over the normal range is usually thought to be good evidence of emphysema, but the assessment of emphysema in the presence of lung fibrosis is exceedingly difficult.

If the disease process is unilateral or different in each lung—that is, collapse or fibrosis with contralateral lung distension—the lung-volume measurements, as obtained by external spirometry, are impossible to interpret. Even if the lung volumes of the separate lungs are obtained by bronchial catheterization, one cannot be certain whether the changes demonstrated are due to actual emphysema or fibrosis or to mechanical events in the chest such as mediastinal shift and collapse. Again, it should be emphasized that it is unwise to regard the various subdivisions of lung volume as a permanent expression of morphological or pathological changes. There can be great changes in the respiratory level (as measured by the functional residual capacity) and the residual volume in the same patient in relatively short periods of time. Exacerbations of bronchospasm and bronchitis will cause considerable but reversible increase of the functional residual capacity and residual volume.

Finally, it can be stated that, although the lung volumes are useful data and represent one of the first attempts to measure disturbances of lung function, they are of very limited value alone, and in our present state of knowledge they can be grossly overinterpreted.

Ventilatory Capacity (Maximum Breathing Capacity)

The lung-volume measurements are entirely spatial and have no relation to time. Thus the vital capacity is a measure of the maximum filling and emptying of lungs, but provides no information whatsoever concerning the speed and efficiency of this filling and emptying during increased ventilation. The ventilatory capacity depends more upon this speed and efficiency than upon the absolute size of the range of movements. The voluntary maximum breathing capacity first introduced by Hermannsen (1933) is of great value in the assessment of ventilatory function. The maximum breathing capacity (M.B.C.) is defined as the maximum volume of air that can be breathed in unit time. It is usually measured for 15 seconds and then converted to litres a minute. It should be emphasized that the ventilatory volumes obtained by maximum voluntary hyperventilation, although a most useful measure of the efficiency of the bellows action of the lungs, far exceed those obtained during the heaviest possible exercise or by maximum respiratory stimulation by increased tensions of carbon dioxide. If the true ventilatory capacity were defined as the maximum volume that can be ventilated in unit time without undue discomfort, then it is usually about half the maximum breathing capacity. The maintenance of a high ventilatory capacity requires good neuromuscular co-ordination (which is rarely affected), even and adequate application of negative pressure to the lung surfaces, a normally patent tracheobronchial tree, normal elasticity and rebound of the lung tissue, and movable components of the chest wall. It is manifest that a large number of important factors are being assessed simultaneously. The prediction formulae of the maximum breathing capacity employ the age and body size (Baldwin *et al.*, 1948) or age alone (Wright *et al.*, 1949). There is a large reduction of maximum breathing capacity as the age increases.

There are two commonly used methods of determining the maximum breathing capacity. In the first and more informative method an ordinary Benedict type spirometer is employed. It is important that the resistance is kept to a minimum, and wide non-corrugated tubing should be employed: 1½-in. (3.8-cm.) tubing is adequate; the use of very wide tubing introduces new errors. The inertia and natural frequency of the system will cause inaccuracies, but if the bell is reasonably light it has been shown (D'Silva and Mendel, 1950) that reliable results can be obtained up to respiratory frequencies of 110 a minute. Other workers measure the maximum breathing capacity with non-return valves each side of the mouthpiece and collect the expired air in a Douglas bag or a Tissot spirometer. It is important that the valves used should have a reasonably low resistance even at very high rates of air flow. This method is particularly useful when dealing with a "mixed" population of tuberculous and non-tuberculous patients. Only the mouthpiece and valves need be cleaned and sterilized, as there is no rebreathing.

In this test the subject is usually told to breathe as deeply and as rapidly as possible. These instructions are self-contradictory, but many authors state that the compromise reached by the patient is his best ventilatory state. There is as yet no proof

of this, and there is in fact good evidence (Bernstein *et al.*, 1952) that unless a respiratory rate of 70 a minute or over is reached low values will be obtained. Emphasis on speed and dictating the rhythm imparts a sense of urgency and need for maximum effort. The personality and power of exhortion of the observer is important, and this factor is another cause of the varying figures obtained in different laboratories. It would be more satisfactory if a standard apparatus and technique could be agreed upon by all workers in the field, but at present this does not seem to be possible. There may be some risk in pulmonary tuberculosis and other chronic infections, such as bronchiectasis, that this highly unnatural and relatively violent respiration will cause aspiration of actively infected material into healthy lung tissue. Although several workers have mentioned this hazard, only to dismiss it, common sense would suggest that the procedure is not without danger. In such instances I have satisfied myself with asking the patient to take a few rapid and forced respirations, using a high-velocity tracing. The ventilatory rate for each breath is measured in litres a minute, and the highest recorded is noted. The comparison of such results with the maximum breathing capacity measured by the usual method in less ill patients has been most satisfactory.

Gaubatz (1938), Tiffeneau and Pinelli (1948), Gaensler (1951), and Kennedy and Stock (1952) have measured the volume of gas expired in standard time during a single forced expiration after filling the lungs. Gaensler employs a spirometer with an automatic timing device so that the volume expired in a fixed time can be measured without a tracing. This is a great advantage in routine clinical work. He has shown an excellent correlation between this "timed capacity" ($\frac{1}{4}$ second) and the maximum breathing capacity.

How is the maximum breathing capacity affected in pulmonary emphysema? It is in this disease, in which the ventilatory capacity is most impaired, that the test is most valuable. It is much more simple than those used to determine the residual volume, and assesses the disability which is the main cause of the patient's dyspnoea and discomfort. One important disadvantage of this method should be mentioned. Bronchospasm, including bronchiolar obstruction due to oedema or secretion, will greatly reduce the maximum breathing capacity, and thus its value as a measure of true emphysema and permanent lung damage is greatly reduced in just those cases in which emphysema threatens and needs to be assessed.

A study of the ventilatory capacity before and after the inhalation of such "antispasmodics" as adrenaline can be carried out in order to assess the separate effect of bronchospasm. However, this is only a crude method, as such a procedure never raises the figure to that obtained if and when the bronchospasm remits naturally.

In patients with generalized pulmonary fibrosis and without emphysema, as judged clinically, radiologically, and by normal or reduced residual volumes, the ventilatory capacity is not greatly impaired. The mean of the maximum breathing capacity in a series of 39 such patients was 78% of the mean of a large group of normal subjects (Baldwin *et al.*, 1949a). Yet the vital capacity of many of these patients was greatly diminished. The decrease of the range of the lung bellows seemed to be compensated by increased efficiency and speed of movement. However, despite their relatively unimpaired ventilatory capacity, many of these patients were dyspnoeic on moderate exertion.

Ventilatory Capacity and Dyspnoea

Cournand and Richards (1941), in order to study the relationships between ventilatory demands and ventilatory capacity, employed a standard step-test of thirty 20-cm. steps in one minute and measured the minute-ventilation during this time and for five consecutive minutes afterwards during recovery. This gave the minute-ventilation during a standard exercise and also allowed the study of the various ventilatory volumes associated with various degrees of dyspnoea. They studied a large group of patients suffering from pulmonary tuberculosis with varying degrees of disease, fibrosis, and collapse. After the step-test 68 patients experienced dyspnoea. During the last minute of dyspnoea the mean minute-ventilatory volume, when expressed as a percentage of the patient's maximum breathing capacity, was 37%. In the minute following relief from dyspnoea the mean ventilation was 29% of the maximum breathing capacity. They emphasized that there was considerable variation in different individuals.

In a later study of patients with generalized pulmonary fibrosis (Baldwin *et al.*, 1949a) a remarkably similar relationship was found. They also reported that the mean minute-ventilation of those with moderate dyspnoea was 49% of the maximum breathing capacity, and with very severe dyspnoea 69%. It was clearly shown that the cause of the dyspnoea in these patients with pulmonary fibrosis was partly the loss of ventilatory capacity and partly the abnormally large volumes ventilated on exercise.

When patients with severe emphysema and very limited ventilatory capacity, as measured by the maximum breathing capacity, were studied many signalled that they were relieved of dyspnoea when the minute-volume fell to 50–60% of the maximum breathing capacity (Baldwin *et al.*, 1949). It has been suggested that the emphysematous patient is grateful for small mercies and regards what, to him, is only moderate ventilatory discomfort as tolerable and not constituting shortness of breath. In any case there is no doubt that these relationships are no longer valid in patients with extremely impaired ventilatory capacities.

Cournand and Richards (1941) termed the unused percentage of the maximum breathing capacity the "breathing reserve" and related this figure to the various degrees of dyspnoea. This term can be criticized, as a large amount of this so-called reserve can never be used. Even a normal subject ventilating 50–60% of his maximum breathing capacity after very violent exertion is uncomfortably dyspnoeic. It cannot be overemphasized that the maximum breathing capacity is only an arbitrary measure of the bellows action of the lungs and does not represent the maximum volume that can be ventilated by that person in response to natural physiological stimuli.

Other workers state the ventilation in any given state as a fraction of the maximum breathing capacity, and call this the "dyspnoea index" (Wright, 1944). It is simpler to state the actual ventilation under any given condition as a percentage of the maximum breathing capacity. This is self-explanatory and avoids the false inference of infallibility associated with the word "index." The term "dyspnoeic index" has been employed (Hugh-Jones and Lambert, 1952) to describe the percentage of the maximum breathing capacity ventilated during a step-test when standard work is performed. The height or the number of steps in unit time are adjusted to standardize the work done with different body weights. The standardization of the amount of work done is of value when studying the ventilatory responses in patients whose weights vary greatly or in the study of ventilatory behaviour in different groups of patients. However, it is undesirable to convert this well-established method of measuring ventilatory discomfort in various degrees of activity into a rigid "index of dyspnoea." The careful elimination of the effect of body weight in assessing dyspnoea in real people with different body weights is also unfortunate. These variable body weights will cause varying ventilation and resultant dyspnoea during any standard activity (walking, stair-climbing, etc.).

It is still not known why a person should be extremely uncomfortable when his physiological demands—for example, exercise—cause him to ventilate about half of the air he can shift at rest, and without distress, by voluntary hyperventilation. There is great need for a more precise study of the ventilatory mechanisms during exercise causing dyspnoea in normal subjects and in those with various lung diseases. The level at which these patients breathe, the range and speed of their respiration, and the movement of the diaphragm and ribs during shortness of breath would not only be of fundamental interest but would bring important knowledge that could be applied to the various collapse and surgical procedures causing reduction of the ventilatory capacity.

Ventilatory Volumes

These can easily be determined by collecting the expired air during various activities. A Douglas bag can be carried by the observer if the patient is walking or going upstairs, and the volume of gas expired during a fixed period be measured by passing the gas collected through a flowmeter or into a Tissot spirometer. Walking on a treadmill or a simple step-test will allow the expired gases to be collected and measured with greater ease, and a gas-meter type of recorder can be used. The disadvantage of the step-test is that the patient is usually not in a stable state, nor can the data be easily related to everyday activities. Many workers take the opportunity of carrying out arterial blood studies during these exercise tests.

Remarkably different ventilatory volumes are obtained in different patients. Many will ventilate only 10 litres a minute while walking at moderate speed, whereas patients are encountered who ventilate as much as 50 litres a minute. The demands on the ventilatory capacity will obviously be very different in two such patients, and, although they may have the same ventilatory capacity, the latter patient will obviously become dyspnoeic with a far less degree of exertion.

Passing from these empirical determinations of ventilatory volumes, let us briefly consider some of the factors that influence the amount of ventilation in various diseases.

In the normal subject about one-quarter to one-third of the inspired air does not pass beyond the passages lined by mucosa (the so-called anatomical dead space) where no significant gas exchange with blood takes place. In many lung diseases this "dead space effect" is greatly increased by the ventilation of unperfused lung tissue, and thus an abnormally large proportion of inspired air takes no part in the removal of carbon dioxide and the oxygenation of blood. This will render larger ventilatory volumes necessary for a fixed task, and this added demand can be ill afforded in the face of reduced ventilatory capacity. In certain lung diseases the changes in the elasticity and physical properties of the lung tissue in certain areas of lung may result in overventilation of the more healthy areas, and this overventilation is also wasteful and will have the same effect as increased dead space.

Secondly, there is the influence of changes in the partial pressure of carbon dioxide in the alveoli and body fluids, which are compensated and perpetuated by similar changes in body base. If the partial pressure of carbon dioxide is lowered by intermittent but repeated hyperventilation on exercise the respiratory centre will become more sensitive to a fixed amount of carbon dioxide produced on exercise, as the resulting increase in H-ion concentration will be greater than normal owing to the decreased buffering effect. These increased ventilatory volumes are necessary to remove a standard amount of carbon dioxide, as the alveolar gas is now relatively poorer in carbon dioxide content. In a number of cases of pulmonary fibrosis, pathological infiltration of lung, and heart failure, the carbon dioxide in the alveoli and blood is much reduced and there is little doubt that this factor is partly responsible for the hyperventilation encountered in these diseases.

If, as in severe emphysema, there is a lag of carbon dioxide excretion on each occasion when the patient exercises, owing to ventilatory disability, there will be a tendency for the partial pressure of carbon dioxide to rise, and if this is increasingly buffered then carbon dioxide retention (compensated gaseous acidosis) occurs. It must be emphasized that the gradient of this gas across the alveolar membrane between blood and alveolar air is unaltered, the partial pressure of carbon dioxide being raised throughout the lungs and body. In such cases the respiratory stimulation by a fixed amount of carbon dioxide is diminished, as the increased buffering will cause less increase in H-ion concentration. It can be shown that there is significantly less ventilation on exercise in this group of emphysematous patients as compared with those without high blood and alveolar carbon dioxide tensions. It has also been suggested that the respiratory centre becomes less sensitive to carbon dioxide and H-ion changes in these cases.

Thirdly, the added anoxic stimulus to respiration is important in certain diseases. Although it is generally known and taught that anoxaemia at rest causes a definite but not very pronounced increase of ventilation, it is less often appreciated that anoxaemia associated with exercise causes a most dramatic increase of ventilation. The increased ventilation caused by anoxaemia at rest washes out carbon dioxide and also reduces the H-ion concentration in the body. Thus two of the normal stimuli to respiration are reduced and the effect of anoxic stimulation is mainly counteracted. If, however, the patient is exercising, and the body carbon dioxide and H-ion concentrations are maintained or increased despite the increased ventilation, then the anoxaemic stimulus becomes more fully apparent (Gray, 1950). This mechanism is particularly important in diseases in which oxygen transfer is inadequate but the ventilatory capacity is but little impaired, as such patients are capable of marked temporary activity, causing abrupt anoxaemia. Good examples of this are certain types of pulmonary infiltration causing difficulty in oxygen transfer across the alveolar membrane (Austrian *et al.*, 1951; Donald *et al.*, 1952). Such patients become anoxaemic and dyspnoeic despite a relatively unimpaired ventilatory capacity. Their dyspnoea is due to the enormous ventilatory volumes that occur with exercise.

Another instructive example is seen in patients with large intracardiac shunts and pulmonary stenosis. On exercising these patients are unable to increase the pulmonary blood flow and oxygen uptake to any appreciable extent, and extreme anoxaemia ensues. Despite their relatively normal lungs and ventilatory capacity they become extremely dyspnoeic owing to their enormous ventilatory volumes—that is, 50–60 litres a minute walking slowly. The low carbon dioxide tension in the body will also contribute to this extreme hyperpnoea.

It is often stated that the Hering–Brauer reflex, causing inspiratory inhibition with a certain degree of lung distension, is increased in activity in many pulmonary diseases, particularly in pulmonary fibrosis. If overactive this reflex causes more frequent and shallow respiration. It is not yet proved that overactivity of this reflex can cause increased total ventilation. There is good evidence that the inhibition of inspiration occurs earlier than normally in the pulmonary congestion of cardiac origin, causing more frequent and shallow respirations, although it is still doubtful whether this is the cause of increased ventilation (Christie, 1932). With regard to the Hering–Brauer reflex being increased by pathological processes or fibrosis in lung disease, this is still only a hypothesis, and no good definitive evidence has yet been forwarded to substantiate it.

Intrapulmonary Gas-mixing

Efficient gas exchange is to a large extent dependent upon the efficient distribution of inspired air to all alveolar spaces. Overventilation of one part of the lung cannot compensate for poor oxygenation in underventilated lung. The haemoglobin is saturated to all intents and purposes by adequate ventilation, and further ventilation will add but little oxygen to the blood perfusing that area. If the tidal air that passes the relatively rigid anatomical dead space is almost equally distributed to all alveoli, as we have good reason to believe is the case in the healthy lung, then it is certain that normal lung will be a remarkably efficient mixer of inhaled gases. Further, if the rate of mixing of inhaled gases is studied, then this will be a useful measure of the efficiency of gas distribution in the lungs. A number of factors that will influence the speed at which an inhaled foreign gas will be mixed throughout the lung spaces can be predicted on first principles—for example, the tidal volume, the size of the rigid anatomical dead space, the functional residual volume, and the rate of respiration (Darling *et al.*, 1944; Birath, 1944).

Cournand *et al* (1941) measured the alveolar nitrogen after seven minutes' quiet oxygen breathing during the determination

of the residual volume. They showed that this was abnormally high in emphysema and attributed this to the inefficient ventilation of many alveoli and air spaces.

Birath (1944) compared the actual mixing curves obtained by serial sampling while breathing a hydrogen mixture with theoretical curves calculated with all the known variables, and assuming mixing to be perfect. Any retardation of mixing, no matter what the cause, was expressed as being due to a certain-sized rigid space between the mouth and properly ventilated lung. If this figure was greater than the accepted size of the normal anatomical dead space, then the excess figure expressed the mixing deficiencies of the lung. This method is unsatisfactory, as the anatomical dead space cannot be accurately measured or foretold even in normal subjects. Other workers (Boothby *et al.*, 1948; Carlson *et al.*, 1948; Fowler and Comroe, 1948) have carried out continuous recordings of the nitrogen washed out and alveolar nitrogen concentration (end of tidal air samples), while breathing oxygen, by means of the Lilly-Hervey nitrogen meter.

As previously mentioned, Meneely and Kaltreider (1941) showed that the rate of helium mixing in emphysema during lung-volume determinations is much reduced. Bates and Christie (1950) studied this phenomenon with greater thoroughness. They determined and corrected the effect of delayed mixing in the circuit and katharometer lag as well as allowing for the known variables already mentioned. No attempt was made to correct for the anatomical dead-space effect. Gross impairment in mixing was demonstrated in a group of emphysematous subjects. They also showed that there was considerable impairment of mixing, even in normal subjects, with increasing age. One asthmatic subject was studied while in severe bronchospasm and on two occasions during his recovery. The mixing efficiency rose remarkably as his bronchospasm abated. It is apparent that, like lung-volume and ventilatory studies, this test is also at the mercy of bronchospasm and bronchial obstruction, and is therefore not a reliable index of permanent lung damage.

All these methods show that the mixing capacity and inspired gas distribution in various lung diseases are impaired and abnormal. However, this disturbance is only assessed as if the lungs were dry unperfused organs. Such an assessment gives no information concerning the relationship of the alveolar underventilation, which is being indirectly demonstrated, to the blood flowing through the lungs. Fowler and Bateman (1950), who have contributed greatly to the study of mixing deficiencies, now feel that the study of the gases encountered in the lungs while breathing air and the correlation of such studies with arterial blood-gas tensions will yield far more valuable data on the real effects of alveolar underventilation. Although hydrogen and helium are excellent gases to demonstrate mixing deficiencies they are light and highly diffusible gases which behave very differently from the gases present in the lungs during ordinary air-breathing. Rauwerda (1946) has produced a valuable monograph on the subject of intrapulmonary gas-mixing.

Respiratory Velocities

The physician of the last century who asked a patient with respiratory disease to whistle or blow a candle out was crudely assessing the maximum respiratory velocities. Sensitive and accurate instruments have been evolved to record instantaneous air-flow velocity (Silverman, 1945). The rate of flow is stated in litres a minute, as the actual velocity recorded is a function of the cross-section of the apparatus where the air flow is being measured. The velocity of flow in the air passages and finer bronchioles, under different conditions and in various diseases, is yet to be determined. Although many workers have obtained records in a number of normal and abnormal subjects under different conditions, little of real significance has emerged from its use. However, this approach is relatively new and may yet yield important findings. It is possible that a simple whistle-like instrument to measure the maximum expiratory velocity will become a standard clinical tool.

Breathing Exercises

Most of us are inclined to believe that breathing exercises are a convenient placebo, and an indirect form of psychotherapy in respiratory conditions where little else can be offered. I would make an exception of post-operative breathing exercises, where the principle of encouraging an early return to full function, in what is usually normal lung, is sound. It must be remembered that these physiotherapy sessions are expensive in personnel, time, and money. It is my belief, although I have no proof, that breathing exercises have no effect whatsoever on emphysema and bronchospasm. Recent studies have shown that physiotherapists and singing teachers have no more control over their diaphragmatic movement than those whom they instruct (Wade, 1951). It is high time that more precise studies of the effect of these procedures on respiratory function were carried out to determine in what type of case, if any, physiotherapy is of value.

Summary

Summarizing this rapid and imperfect survey of spirometric methods relating to the efficiency of ventilation, I would like to repeat that in the past too much emphasis has been laid on the static aspects of the lung volumes. It is more important to determine the ventilatory capacity of the lungs by such simple tests as those described and then to determine what ventilatory demands will be encountered in conditions that simulate normal activities as closely as possible. The factors that increase these ventilatory demands in various diseases have not been adequately studied. Finally, I would state that if I could have only one figure in a case of emphysema, although I should like many more, I would ask for the maximum breathing capacity.

THE PULMONARY CIRCULATION

Let us next consider the haemodynamics of the pulmonary circulation, particularly the flow and pressure relationships. The important aspects of the relationships of alveolar circulation to ventilation will be considered separately. It has long been a matter of debate whether the pressure and volume variations in the pulmonary circulation are the passive result of conditions imposed upon it by respiration and the systemic circulation or whether there is active vasometricity of pulmonary vessels. Except for transient differences, the blood flow through the lungs is equal to that through the whole systemic circulation. However, despite this, the pressures in the lesser circulation are of a far lower order than those in the systemic circulation. The short, distensible, and capacious pulmonary arteries, arterioles, and pre-capillaries, and the enormous network of large pulmonary capillaries surrounded by air, allow the whole cardiac output to flow through the pulmonary vascular bed with a pressure head of only one-sixth of that in the systemic circulation.

The introduction of the technique of cardiac catheterization has made it possible to study the pulmonary circulation in both normal and abnormal subjects without any great disturbance of physiological status. Many normal subjects have now been investigated under near basal conditions, and the upper limit of normal pulmonary artery systolic pressure is believed to be 30 mm., of mean pressure 15 mm., and of diastolic pressure 10 mm. Hg. These pressures are measured from the level of the right atrium, and are the mean of the values throughout a full respiratory cycle.

Riley *et al.* (1948) studied the effect of exercise on the pulmonary artery pressures in three normal subjects. Resting studies were carried out with the subjects lying supine and exercise studies while riding a bicycle ergometer in the upright position. It was shown that, even though the oxygen consumption increased sixfold and the cardiac output more than doubled, the pulmonary artery pressure did not alter significantly. The resistance of the pulmonary vascular bed to this increased flow was greatly diminished on exercise, being only a third of the resistance at rest. As a result of this, the work of the right ventricle against pressure was only doubled; whereas that of the left ventricle was trebled. Hickam and Cargill (1947) obtained similar results, although their subjects did not increase their oxygen uptake and cardiac output to the extent of Riley's subjects. Both these groups of workers pointed out that the decrease of pulmonary resistance could not be explained by the passive

dilatation of the vascular bed, but that there must be independent and active widening of the vessels, or the opening up of new channels. Dexter *et al.* (1951) have shown that if normal subjects are exercised in the supine position so that the oxygen consumption exceeds 400 ml. per m.^{2} of body surface, per minute, then a slight but significant rise of the pulmonary artery pressure occurs. They found that under these conditions the pulmonary resistance showed little alteration during exercise. These different findings may have been due to errors of pressure-recording in the erect position or as yet undemonstrated differences in intrapleural pressures while exercising in the supine and erect positions.

This demonstration that the pulmonary vascular bed is a low-resistance low-pressure system both at rest and with exercise is important. Not only is it advantageous from a purely mechanical aspect, but these properties of the lung vessels will allow considerable restriction of the vascular bed by resection or disease without marked pulmonary hypertension or right ventricular embarrassment.

Motley *et al.* (1947) have convincingly demonstrated that a rise in the pulmonary artery pressure is rapidly induced in normal subjects by breathing 10% oxygen for a short period of time (ten minutes). The average rise in mean pulmonary artery pressure in five subjects was from 13 to 22 mm. Hg. This increased pressure could not be attributed to increase in flow, as the cardiac output was but little altered. More recent experiments (Cournand, 1950) show that there is, in fact, some increase of cardiac output under these conditions, but that this increase is of such an order that it could have little effect on the pulmonary artery pressure. The work of Dexter *et al.* makes it necessary to review the accuracy of this statement, but it would seem to be still valid. Drinker (1945) has demonstrated that anoxia can cause altered capillary permeability, oedema, stasis, and perhaps increased resistance. However, the almost immediate reversibility of the rise in pulmonary artery pressure due to anoxia makes this hypothesis unlikely. There is no good evidence of left ventricular failure with back pressure. Wade, Cumming, and I (1951, unpublished observations) have measured the pulmonary "capillary" pressure, a crude transpulmonary measurement of pulmonary venous pressure obtained by occluding a branch of the pulmonary artery with the tip of the cardiac catheter, in several subjects with normal cardio-respiratory systems, while breathing air and 10% oxygen, and no significant change in this pressure was recorded. The only feasible explanation of the rise in pulmonary artery pressure when breathing low tensions of oxygen is that there is active constriction of pulmonary vessels.

Liljestrand and von Euler (1946) demonstrated that moderate anoxia caused pulmonary hypertension in intact cats. They produced good evidence that this rise in pressure was due to the direct action of low oxygen tension upon the tone of the arterioles or pre-capillaries. They did not believe that it was due to nervous influences, increased flow, or increased back pressure. It was suggested that this local anoxic action would result in an exquisite control of alveolar circulation, causing blood to flow to the areas where efficient ventilation and normal oxygen tensions were present.

Pulmonary Circulation in Lung Disease

As the only reliable method of studying the haemodynamics of the pulmonary circulation in lung disease is by cardiac catheterization, the present knowledge is still very scanty. In one of the earliest studies (Riley *et al.*, 1948) a very heterogeneous collection of lung diseases was investigated. The diagnosis included pulmonary fibrosis, bronchiectasis, emphysema, and silicosis with tuberculosis. Most of these patients were unable to exercise vigorously. Even in these severe, chronic, and disabling respiratory diseases the pulmonary artery pressures were normal or but little raised while at rest, and showed only a moderate rise above normal when the patients exercised. Those who suffered the greatest rise of mean pulmonary artery pressure—that is, 13 to 42, 23 to 42 mm. Hg.—on exercise also showed a significant degree of arterial blood desaturation. However, even those who did not develop arterial hypoxaemia showed some abnormal rise of pressure, and it seemed that the pulmonary vascular bed was no longer capable of accommodating increased flow without some rise in pressure.

Pulmonary Emphysema

The piecing together of the natural history of pulmonary hypertension and right ventricular hypertrophy and failure in this disease requires ventilatory and arterial blood studies, and cardiac catheterization of a large number of patients over long periods. I am particularly grateful to Drs. Harvey, Ferrer, Richards, and Cournand (1951) for allowing me to use, before publication, some of the results in the largest series yet studied, of which I have some personal knowledge.

The first group studied consisted of mild to moderate cases of emphysema as judged clinically and radiologically. Their residual volumes were increased and the ventilatory capacity greatly impaired. There was no significant degree of arterial blood oxygen desaturation (90% or above) and the standard step-test did not cause any fall in arterial oxygen saturation below this level. None of these patients showed any rise of pulmonary artery pressure or circulatory abnormality while at rest. A few who were exercised showed a moderate increase in pulmonary artery pressure. Such a finding in the absence of arterial hypoxaemia would suggest that the pulmonary vascular bed was unable to accommodate the increased flow with exercise without a rise in pressure. This would further suggest that the pulmonary bed is damaged and restricted in this disease.

In the second group studied the emphysema was more severe, as judged clinically and radiologically and by the increase of residual volume and impairment of ventilatory capacity. All these patients showed considerable arterial blood desaturation on exercise and most of them had carbon dioxide retention (high arterial pCO_2). As in the previous group, none had a history suggesting right heart failure. Only moderate pulmonary hypertension was found, the mean pulmonary artery pressure at rest being about 25 mm. Hg. There was no alteration of the size of the heart or of the pulmonary arteries. Electrocardiographic studies, using the criteria of Goldberger (1944), Wilson *et al.* (1947), and Myers *et al.* (1948), showed no evidence of right ventricular hypertrophy. The cardiac output, total blood volume, and haematocrit reading were slightly raised. There are no reports of the effect of exercise in this type of patient, although a few that I have catheterized have shown a considerable rise of pulmonary artery pressure.

Lastly, there is the group of emphysematous patients in congestive heart failure (cor pulmonale). Almost without exception the failure had been precipitated by an acute anoxic episode such as severe bronchitis or pneumonia. All these patients had severe pulmonary hypertension (around 50 mm. Hg mean pressure) and extreme arterial blood oxygen desaturation (50 to 60% saturation). Polycythaemia was pronounced and the total blood volume was increased. These patients had large right ventricles and the electrocardiogram showed marked right ventricular hypertrophy. These electrocardiographic findings are a measure of muscle mass, and one must conclude that hypertrophy had been present for some time. In most of these cases the cardiac output was high or high normal. The few patients who had low cardiac outputs in this state did not recover.

When these patients responded to treatment such as oxygen therapy, antibiotics, aerosol inhalations, and "antispasmodics" to improve ventilatory function, and mersalyl, digitalis, and bleeding to relieve the circulatory embarrassment, and were again studied, a surprising series of findings emerged. The pulmonary artery pressure dropped to very moderate and, in some cases, near normal figures. The respiratory function, as judged by arterial percentage haemoglobin saturation, lung volumes, and ventilatory capacity, was also greatly improved. In fact, after recovery from heart failure these cases were almost indistinguishable from the previous group, who had very mild pulmonary hyper-

tension and no evidence of right heart hypertrophy or insufficiency. A number of patients who had had right-sided heart failure, and had recovered, showed similar findings. The blood volume was significantly raised, and there was of course evidence of right ventricular hypertrophy. This marked fall in pulmonary artery pressure on recovery is probably due to relief of the anoxic vasoconstriction, decrease in the blood volume and viscosity, and the reduction of cardiac output. Thus the old concept that right-sided heart failure in these patients is mainly due to irreversible structural damage to pulmonary vessels can no longer be supported. Prompt and active therapeutic measures are life-saving and cause a dramatic reversal of many of the most adverse factors.

Although many cases of severe emphysema are under medical supervision over long periods, it is most unusual for one of these patients to develop a large heart with right ventricular hypertrophy and, finally, failure while under observation. In fact, practically all patients with cor pulmonale due to emphysema are seen for the first time when they are, or have recently been, in heart failure and already have right ventricular hypertrophy. Further, when these patients are studied after recovery a number show a smaller degree of pulmonary distension and a better ventilatory capacity than severely emphysematous patients without cardiac involvement.

I would like to offer a tentative explanation of these facts. If a patient with emphysema suffers from severe ventilatory disability, then this of itself may protect the right ventricle by greatly limiting activity and any resultant pulmonary hypertension due to increased blood flow and, perhaps, severe anoxia. Thus right ventricular hypertrophy and dilatation, which in some ways is the "beginning of the end," does not develop. However, those patients with less ventilatory impairment are not so limited in their activities and are able, without intolerable ventilatory discomfort (dyspnoea), to carry out regularly enough exercise to cause pronounced pulmonary hypertension. Thus right ventricular hypertrophy may develop and any sudden further stress due to infection or added anoxia may cause failure.

Although ventilatory studies help to measure dyspnoea, the most important symptom and disability so far as the patient is concerned, the circulatory aspects of this disease must also be studied, especially when prognosis is being considered. Clinical examination, electrocardiography, and screening make this assessment relatively easy in most cases, without cardiac catheterization, which should be reserved for those who are studying the disease, as well as the patient. Even in cases with moderately good ventilatory function, if there is right ventricular hypertrophy then there is constant danger of heart failure that may be precipitated by one of the almost inevitable respiratory infections that are a feature of this disease. At present there is no general agreement as to whether patients with emphysema should restrict their activities or not. It would be of great use to know whether elaborate and unremitting therapy to improve alveolar ventilation, in an attempt to avoid anoxaemia and pulmonary hypertension, is really worth while. Further work is needed to clarify such problems so that the clinician is better equipped to advise the patient with emphysema.

Pulmonary Fibrosis

Up to the present pulmonary circulatory studies have been carried out in very few cases of generalized pulmonary fibrosis. Any attempt to assess the disability and prognosis in occupational lung fibrosis must include a thorough study of the effect of the disease upon the pulmonary circulation and the right heart. Electrocardiographic studies are not enough, and the development of pulmonary hypertension, and its relation to exercise, must be determined. In view of the fact that the ventilatory capacity is often not greatly restricted, the safety of encouraging men with pulmonary fibrosis to increase their activity, and even carry out hard physical tasks, should be more carefully considered.

[Part II, with a list of references, will appear in our next issue.]

SYMPATHETIC NERVES AND ECLAMPSIA

BY

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It is the rule, rather than the exception, for a woman who suffers from eclampsia at the end of her first pregnancy to have normal subsequent confinements. The earlier the onset of hypertension and proteinuria during pregnancy the more likely is the patient to suffer the same sequence of events in succeeding pregnancies. The onset of this so-called toxaemic state at or about the 30th week of pregnancy is often associated with an unduly small foetus, which does not appear to grow, and which is prone to die *in utero*, with or without evidence of ante-partum haemorrhage.

These facts are illustrated by the following two case histories; several others could be cited.

Case I.—The patient was aged 36 in 1949. *First pregnancy, 1941:* eclampsia at 32nd week; stillborn premature infant. *Second pregnancy, 1944:* eclampsia at 32nd week; S.B. premature infant. *Third pregnancy:* last menstrual period (L.M.P.) March 4, 1949; expected date of delivery (E.D.D.) November 12. On May 26 the blood urea was 20 mg. per 100 ml.; urea concentration, 4.4%; intravenous pyelogram, normal. No abnormal cells discovered in urine. July 5: booked; B.P., 130/80 mm. Hg; urine, N.A.D.; weight 11 st. 6 lb. (72.6 kg.). September 1: 26 weeks pregnant; urine, N.A.D.; B.P., 140/90. From September 1 to October 10 the B.P. varied between 140/90 and 170/120; no proteinuria. October 11: B.P., 180/130; proteinuria; oedema; weight, 13 st. 3 lb. (83.9 kg.). October 19: 32 weeks pregnant; alb.,* 11 parts; oedema; emesis. Caesarean section: male infant, 4 lb. 3 oz. (1.9 kg.), died from pulmonary atelectasis. November 25: B.P., 140/70; urine, N.A.D.; very well.

This patient, influenced largely by her doctor and her husband, refused to have her iliac vessels denervated and asked instead to be sterilized.

Case II.—This patient, aged 25, had Raynaud's disease. Bilateral cervical sympathectomy had been successfully carried out in 1950.

First pregnancy, 1949 (in Sunderland): 30th week. B.P., 166/110; alb., 2–8 parts; oedema of ankles. April 3: spontaneous delivery; stillborn (S.B.) foetus, 3 lb. 2 oz. (1.4 kg.). *Second pregnancy, March, 1950:* an abortion. *Third pregnancy, 1951:* L.M.P., February 27; E.D.D., December 6. May 29: 12–14 weeks pregnant; B.P., 100/64; urine, no protein; weight, 8 st. (50.8 kg.); Hb, 65%. From May 29 to August 17 the B.P. varied between 110/66 and 120/80. August 25: admitted with B.P. of 150/100; no proteinuria. B.P. then varied between 140/90 and 156/90; no symptoms. September 17: sudden appearance of 6 parts of albumin in urine; oedema; B.P. rose to 170/120; weight, 8 st. 5 lb. (53 kg.). September 29: spontaneous breech delivery; S.B. macerated foetus, 2 lb. 6 oz. (1.1 kg.). October 7: B.P., 104/76; trace of albumin in urine. October 9: B.P., 150/110; trace of albumin in urine; recurrence of symptoms of Raynaud's disease.

Such cases are not common, but they demonstrate that women without detectable stigmata of the cardiovascular–renal system may develop recurrent hypertension, proteinuria, oedema, and other symptoms at about the 30th week of pregnancy in spite of the most careful antenatal care.

*Alb.=proteinuria expressed in parts recorded in Esbach's albuminometer.

Apart from the preparations women may get from the food office, each who attends the antenatal clinic receives :

Tabellae ferri sulphatis compositae (*N.F.*), 1 tablet thrice daily. Each tablet contains exsiccated ferrous sulphate, 3 gr. (195 mg.), copper sulphate, 1/25 gr. (2.4 mg.), and manganese sulphate, 1/25 gr. (2.4 mg.).

Tabellae calcii cum vitamino D (*N.F.*), 1 tablet thrice daily. Each tablet contains calcium sodium lactate, 7½ gr. (488 mg.), calcium phosphate 2½ gr. (163 mg.), and calciferol 1/4,800 gr. (0.014 mg., which is equivalent to 500 international units of vitamin D).

Those in the antenatal ward are given :

Tabellae ferri sulphatis compositae (*N.F.*), 2 t.d.s.
Tabellae calcii cum vitamino D (*N.F.*), 1 t.d.s.
Vitamin B_1, 3 mg. t.d.s.
Vitamin C, 25 mg. t.d.s.
Capsules containing 4,500 units of vitamin A and 450 units of vitamin D, 1 t.d.s.

Case II was also given stilboestrol, 5 mg. t.d.s., working up to 30 mg. daily from the time that she booked. She was seen by me almost every week, and put on only 5 lb. (2.3 kg.) in weight.

A number of gynaecologists have attributed eclampsia and pre-eclampsia to abnormalities in the haemodynamic balance (Beker, 1925, 1948; Page, 1939; Bouwdijk Bastiaanse and Mastboom, 1950). Bartels (1928) and Wettley (1938) reported that the vascular system was hypoplastic in a high proportion of fatal cases of eclampsia. Kellogg (1945), Newell and Smithwick (1947), and Peet and Isberg (1949) have recorded successful pregnancies following lumbar sympathectomy, but they were dealing with hypertension of the order of 196/130, and were mainly concerned in lowering the systemic blood pressure.

Since 1930 I have maintained that eclampsia is due to faulty nutrition, together with the mechanical disadvantages which are inevitably associated with the pregnant state. It occurred to me that denervation of the internal iliac vessels might in certain cases improve the blood supply to the placenta and prevent the recurrence of toxaemic symptoms in succeeding pregnancies. This procedure, if effective, might operate : (1) by increasing the blood supply to the uterus ; (2) by cutting off afferent and efferent impulses travelling from and to the uterus along sympathetic pathways.

The possible significance of afferent nervous impulses travelling from the uterus is suggested by the following facts. (*a*) Afferent nervous impulses occasioned by attempts at lumbar puncture in the dog provoked inhibition of water diuresis and proteinuria (Theobald, 1934). (*b*) The painless introduction of a small dilator through the internal os uteri of a conscious patient and the dilatation of the cervical canal under general anaesthesia may cause the blood pressure to rise by some 10 mm. Hg. Traction on the obstetric forceps during delivery commonly causes a rise in blood pressure which may on occasion exceed 60 mm. Hg. Conversely, cauterization of the uterus by the silver stick may cause a fall of blood pressure from 120/80 to 70/40, a pulse rate of 40, emesis, and a cold sweat. All these phenomena may occur apart from pain (Theobald, unpublished observations).

Lastly, it may be recalled that Franklin and Sophian (1949) and Franklin (1951) advanced the hypothesis "that toxaemia of pregnancy is, or includes, a progressively increasing tendency for the renal shunt to be brought into operation, and that fatal bilateral cortical necrosis is the maximal, irreversible result of this tendency."

The Operation

The abdomen is opened by a midline subumbilical incision, the intestines packed off, and the peritoneum divided to expose the bifurcation of the right common iliac artery. This is cleaned with scissors and gauze dissection. Approximately the first 1½ in. (3.8 cm.) of the internal iliac artery is stripped and denervated and the corresponding portion of the internal iliac vein is then treated in like manner. After this procedure has been carried out on the left side the abdomen is closed. It must be observed that the proximal portions of the external iliac vessels are inevitably denervated.

The first two operations were performed in January, 1950, but the original patient has not yet become pregnant. In subsequent operations the stripping of the internal iliac vessels was more extensively carried out so that the obliterated hypogastric arteries were cleaned. Large amounts of nervous and other tissue removed from the blood vessels were fulgurated with the diathermy point. In some cases presacral neurectomy was performed before the abdomen was closed.

The operation is tedious, and the only danger is from haemorrhage, particularly when cleaning the veins deep down in the pelvis. Of the seven patients on whom I have operated only three have become pregnant; their histories are here reported.

Case A

This patient was aged 33. I have looked after her in all three pregnancies.

First pregnancy, 1947.—L.M.P., October 4, 1946 ; E.D.D., July 11. February 11: booked ; 18 weeks ; B.P., 140/90. April 24: 28 weeks ; B.P., 200/130 ; alb., 6 parts ; admitted. In addition to the routine dietetic and hygiene treatment, paravertebral blocks on both sides were carried out on several occasions during the first week. April 30:—eyes: right disk, physiological cupping, exudate, haemorrhage ; left disk, normal. Headache, vomiting, epigastric pain. Morphine regime. May 16: slight accidental haemorrhage ; B.P., 230/130 ; alb., 4 parts. May 17: intrauterine death of foetus. May 23: B.P., 170/110 ; alb., 4 parts ; general condition improved. May 24: delivery, following induction of labour, of S.B. male foetus, 2 lb. 8 oz. (1.1 kg.). It was some weeks before the urine became protein-free. The B.P. subsequently varied for some months between 145/85 and 165/120.

Second pregnancy, 1948.—L.M.P., March 25 ; E.D.D., January 1, 1949. July 6: 12 weeks ; B.P., 130/80–122/94 ; weight, 9 st. 1 lb. (57.2 kg.). August 23: B.P., 170/110 ; alb., 1 part ; weight, 9 st. 6 lb. (57.3 kg.) ; admitted. During the seven weeks in the antenatal ward the blood pressure varied between 140/90 and 170/120. The protein disappeared from the urine, but recurred, although it did not exceed ½ part. The secretion of urine was poor and varied between 20 and 60 oz. (570 and 1,700 ml.) in 24 hours. October 9: intrauterine death of foetus. October 16: spontaneous delivery of S.B. male macerated foetus, 3 lb. 14 oz. (1.8 kg.).

Denervation of the internal iliac vessels, appendicectomy, and partial resection of right ovary were carried out on January 24, 1950. The internal iliac vessels were noticeably small—approximately half the normal size.

Third pregnancy, 1951.—L.M.P., September 5, 1950 ; E.D.D., June 12, 1951 ; weight, 8 st. 13 lb. (56.7 kg.). The blood pressure varied between 120/74 and 138/84 throughout the antenatal period until the 37th week. No proteinuria was detected. Admitted to ward in 37th week. B.P., 150/90 ; weight, 11 st. 1 lb. (70.3 kg.). B.P. settled in ward to 130/90. June 11: induction of labour ; quinine ;

artificial rupture of membranes (A.R.M.); oxytocin drip. June 13: female infant, 6 lb. 7 oz. (2.9 kg.). B.P. rose during puerperium to 160/105 and then returned to normal.

Case B

This patient was 38 years old.

First pregnancy, 1941.—Pregnancy "injected away" at 20 weeks because of "kidney trouble and blood pressure."

Second pregnancy, 1943.—Seventh month; premature S.B. foetus; "kidney trouble and blood pressure."

Third pregnancy, 1950.—L.M.P., November 12, 1949; E.D.D., August 19, 1950. February 2: 12 weeks; B.P., 150/90. March 8: 17 weeks; B.P., 110/70; weight, 9 st. 12 lb. (57.5 kg.); Hb 100%. From March 8 to June 17 the B.P. varied between 100/60 and 120/80. She then developed hypertension and proteinuria, and was kept in bed at home by her doctor. July 1: admitted to ward; B.P., 168/100. In the ward B.P. varied between 130/84 and 200/120, but during the last two weeks was in the neighbourhood of 160/120. Proteinuria, alb., 2½ parts. Maximum weight, 11 st. (69.9 kg.). August 1: spontaneous delivery of macerated female child, 4 lb. 10 oz. (2.1 kg.). Very small placenta. This patient took cod-liver oil, orange juice, iron, and calcium from the very beginning of pregnancy, and stilboestrol in the antenatal ward. August 26: B.P., 180/100.

Denervation of internal iliac vessels, presacral neurectomy, and partial resection of left ovary were performed on October 24, 1950.

Fourth pregnancy, 1951.—L.M.P., March 24; E.D.D., December 31. June 19: 12–14 weeks pregnant; B.P., 110/70; weight 9 st. 2 lb. (58.1 kg.); Hb, 75%. July 27: went cycling in Scotland. B.P. throughout pregnancy, until 36th week, varied between 110/70 and 120/80. November 30: 36 weeks; admitted, as she lives in the country; B.P., 136/90. During second week in hospital B.P. varied between 110/70 and 120/80. Labour induced at 38 weeks, as baby was considered "large enough." December 17: male infant, 7 lb. 8 oz. (3.4 kg.); weight, 11 st. 6 lb. (72.6 kg.); Hb, 75%.

Case C

Infertility patient, aged 40, married 14 years.

First pregnancy, 1949.—L.M.P., June 7; E.D.D., March 24, 1950. October 4: 12–14 weeks pregnant; B.P., 120/80; weight, 9 st. 10 lb. (61.7 kg.). November 30: 22 weeks; B.P., 170/110; alb., ++; oedema, ++; weight, 11 st. 4 lb. (71.7 kg.). Admitted. B.P., 214/120; alb., 4 parts; a few granular and hyaline casts, and red blood cells in urinary deposit; oedema of face, pitting oedema of knees; short of breath; eyes—striated greyish disks, white streaks along main vessels. "Proctocaine" was injected into broad ligaments, 6 ml. on each side. Morphine regime. December 13: blurred, misty vision; everything looked like a shadow; left eye mainly involved; weight, 10 st. 9 lb. (67.6 kg.). December 14: some oedema of retinae; tortuous vessels. December 28: intrauterine death of foetus. January 7: macerated male foetus, 3 lb. 8 oz. (1.6 kg.).

During her five weeks in hospital the blood pressure at first fell slightly, then rose steeply to 230/170. It then became stabilized at about 190/110–220/130, falling in the last week to 160/100–180/120. The blood urea reached a maximum of 30 mg. per 100 ml. Proteinuria varied from 0.5 to 4.5 parts, Esbach. The remarkable feature of this case was the constant excellent output of urine throughout her time in hospital, which reached the level of 205 oz. (5,825 ml.) in 24 hours. This in no way suggested the "Oxford shunt." On January 24 Mr. Ivor Lloyd reported as follows: "Both eyes show severe hypertensive and albuminuric retinopathy with papilloedema. I fear, however, that the retinal changes indicate severe damage to the vascular system and the kidneys, and the prognosis, as judged from the ophthalmic point of view, is not good. The blood pressure was 160/90." On November 20, 1950, the urea clearance was 142% of normal. The electrocardiogram showed the usual pronounced left axis deviation of hypertension.

On February 12, 1951, denervation of internal iliac vessels and presacral neurectomy were carried out. Congenital absence of the left kidney was noted.

Second pregnancy.—L.M.P., August 30, 1951; E.D.D., June 6, 1952. November 19: B.P., 140/90—occasional beat at 170; weight, 9 st. 9 lb. (61.2 kg.). February 13: 24 weeks; B.P., 126/76, this was the only low reading; weight, 9 st. 12 lb. (62.6 kg.). The patient was nervous, not very co-operative, and always feared the worst. Her weight remained almost constant at 9 st. 12 lb. (62.6 kg.) for over four months. She did not look well. No proteinuria. April 9: B.P., 138/96; weight, 10 st. 7 lb. (66.7 kg.); looked better; no proteinuria. April 23: B.P., 170/106; weight, 10 st. 12 lb. (68.9 kg.); admitted; no proteinuria. April 29: B.P. had varied since admission from 150/84 to 160/100; alb., 0.5 part; foetal heart irregular. In view of the irregular foetal heart caesarean section was performed. Female infant, 5 lb. 2 oz. (2.3 kg.). On May 9 Mr. Ivor Lloyd reported: "Bilateral retinal arteriosclerosis and early retinopathy." After delivery the B.P. varied between 110/70 and 138/90. Apart from the temporary recurrence of an anxiety state the mother did well. The baby flourished.

Denervation of the Aorta, Inferior Vena Cava, and Left Iliac Vessels by Means of 5% Phenol Solution

In view of the above results it was decided to determine whether hypertension and proteinuria, once established during pregnancy, could be affected by a comparable procedure.

A primigravida aged 26 was admitted as an emergency case. E.D.D., September 17, 1951. June 28: B.P., 190/100; alb., 4 parts; blood urea, 40–65 mg. per 100 ml.; maximum concentration of urea, 2%; some oedema; foetal heart very irregular. July 3: an incision was made through the left loin, the dissection remaining retroperitoneal. The left common iliac artery and vein, the lower part of the abdominal aorta and inferior vena cava (as it was impossible to expose the right common iliac vessels without making another incision), and the left ureter were generously painted with a 5% solution of phenol: the exposed portion of the left lumbar sympathetic chain was coagulated by diathermy. The patient made an excellent recovery from the operation. From July 4 to August 17 the B.P. varied from 150/100 to 200/120; alb., 2–9 parts. August 18: labour induced at 36th week. August 19: female infant, 2 lb. 14 oz. (1.3 kg.); 36 weeks' gestation; died shortly after delivery. Numerous infarcts in the placenta. May 2, 1952: B.P., 110/76; some protein was still present in the urine.

The abdomen became extremely distended during the last few weeks of pregnancy owing to gaseous distension of the bowel, which took some time to disappear and was still present when she left hospital. It is reasonable to suppose that this distension was due to damage done to the autonomic nervous system by the phenol solution.

Water Diuresis

A Balloon in Uterus.—A rubber balloon was introduced into the uterus a few days after delivery and distended with water to a pressure of 70 mm. Hg, so that it could be felt as a tensely cystic mass reaching 3 in. (7.6 cm.) above the symphysis pubis. The distension of the uterus so occasioned did not seem to affect water diuresis, not even when a weight of 1½ lb. (0.68 kg.) was attached to the end of the balloon.

Faradic Current to Cervix Uteri.—The cervix uteri was stimulated by a faradic current which was just appreciated but did not cause pain. This procedure was tried on three patients and in no way affected water diuresis.

Normal Confinements following the Pre-eclamptic Syndrome Occurring in Pregnancy

During the past five years the few cases in which normal confinements have followed pregnancies in which the pre-eclamptic symptomatology occurred at or about the 30th week of pregnancy have been collected. They number four in all, with a doubtful fifth case (Case 5).

Case 1.—Patient aged 42, Rh-negative. *First pregnancy, 1950:* hypertension, 130/90 to 160/124; alb. varied from 0 to 1 part; usual antenatal treatment and stilboestrol; in antenatal ward five weeks. June 15, 1950: macerated female foetus, 2 lb. 6 oz. (1.1 kg.). The maternal weight increased from 7 st. 11 lb. to 8 st. 2 lb. (49.4 to 51.7 kg.). *Second pregnancy, January 9, 1951:* spontaneous delivery, female infant, 7 lb. 6 oz. (3.3 kg.). Normal pregnancy.

Case 2.—Patient aged 21. November 6, 1950: antepartum haemorrhage at home; B.P., 160/110; alb., 22 parts. November 15: severe frontal headache, photophobia. Caesarean section, male infant, 3 lb. 6 oz. (1.5 kg.), died two days later. *Second pregnancy:* slight oedema up to knees and puffiness of face. Neither hypertension nor proteinuria. February 4, 1952: female infant, 5 lb. 6 oz. (2.4 kg.), delivered at term.

Case 3.—Patient aged 28. *First pregnancy, 1951:* normal until 32nd week, then B.P. 160/100; alb., 4–5 parts. Eleven days later: headache; vomiting; B.P., 180/120; alb., 24 parts; male infant, 5 lb. 3 oz. (2.3 kg.); (36 weeks) did well. When she left hospital the B.P. was still elevated and there was 1 part of albumin in her urine. *Second pregnancy* normal in every respect, except that her blood pressure was 150/90 when she booked. This was the only abnormal reading. June 18, 1952: male infant, 7 lb. 12 oz. (3.5 kg.).

Case 4.—Patient aged 26. *First pregnancy:* booked September 12, 1950; weight, 8 st. 2 lb. (51.7 kg.); B.P., 100/60. December 28: B.P., 180/140; alb., 14 parts; generalized oedema; admitted. No improvement in antenatal ward. January 1, 1951: 30 weeks pregnant; induction of labour; male infant, 3 lb. 9 oz. (1.6 kg.); died aged 24 hours. *Second pregnancy:* E.D.D., August 8, 1952. Normal pregnancy; highest B.P., 140/80; September 9, 1952: male infant, 9 lb. (4.1 kg.).

Case 5.—Patient aged 37. *First pregnancy:* ? hypertension and proteinuria at 36 weeks; male infant, 4 lb. 8 oz. (2 kg.), died. *Second pregnancy:* twins induced at 26th week. S.B., 1 lb. 8 oz. and 2 lb. 4 oz. (0.68 and 1 kg.). *Third pregnancy, 1946, St. Luke's Maternity Hospital:* Normal pregnancy. Female infant, 8 lb. 8 oz. (3.9 kg.). *Fourth pregnancy, May 5, 1952:* Normal pregnancy; female infant, 7 lb. 6 oz. (3.3 kg.).

Living Children, but Not Quite Normal Pregnancies, following Pre-eclamptic Symptomatology

Case 6.—Patient aged 25. October 5 to November 10, 1949: hypertension, 150/100 to 170/120; alb., 2–14 parts. November 10: female infant, 4 lb. 15 oz. (2.2 kg.); died of bronchopneumonia. *Second pregnancy:* B.P. varied between 120/80 and 146/110; alb., 1–3 parts. February 5, 1952: male infant, 8 lb. 8 oz. (3.9 kg.).

Case 7.—Patient aged 27. *First pregnancy, 1947:* abortion at 11 weeks. *Second pregnancy, 1950:* emergency admission in premature labour with transverse lie; B.P., 140/108 to 160/110; alb., 14–16 parts; granular + hyaline casts, many red cells; papilloedema. June 20: S.B. female foetus, 3 lb. 5 oz. (1.5 kg.). September 8, 1951: B.P., 130/76; urine, no protein. *Third pregnancy:* hydramnios; B.P., 120/76–140/94; alb., 0.5 to 2 parts. March 16: breech, male infant, 7 lb., 6 oz. (3.3 kg.).

Case 8.—Patient aged 31. All confinements except the first in this hospital. *First pregnancy, 1941:* ? eclamptic fits; 3 lb. 8 oz. (1.6 kg.) baby; died same day. *Second pregnancy, 1942:* hypertension up to 180/110; alb., 15 parts; S.B. infant. *Third pregnancy, 1943:* hypertension up to 150/100; no proteinuria; infant weighed 4 lb. (1.8 kg.); died after 36 hours. *Fourth pregnancy, 1944:* hypertension up to 150/95; infant, 4 lb. (1.8 kg.); lived a few hours. *Fifth pregnancy, 1947:* hypertension up to 150/85; infant, 7 lb. 12 oz. (3.5 kg.); did well. *Sixth pregnancy, 1949:* hypertension up to 176/100; no proteinuria; baby, 7 lb. 4 oz. (3.3 kg.). *Seventh pregnancy, 1951:* hypertension; alb., 7 parts; ante-partum haemorrhage; placenta praevia; caesarean section; male infant, 5 lb. 3 oz. (2.4 kg.); did well (37 weeks' gestation). It will be noted that, with the exception of the second pregnancy, all the infants were born alive.

Case 9.—Patient aged 28. *First pregnancy:* hypertension up to 160/118; no proteinuria; forceps; male infant, 9 lb. 3 oz. (4.2 kg.); maternal weight, 13 st. to 13 st. 9 lb. (82.6 to 86.6 kg.). *Second pregnancy:* hypertension, 170/120; alb., 12 parts; headache; dizziness; poor secretion of urine; caesarean section at 36 weeks; female infant, 6 lb. 14 oz. (3.1 kg.). Maternal weight: 14 st. 12 lb. (94.3 kg.) at 17 weeks, 17 st. 2 lb. (108.9 kg.) when delivered. *Third pregnancy:* emergency admission; B.P., 140/100; renal glycosuria; no proteinuria; caesarean section; male infant, 8 lb. 8 oz. (3.9 kg.). Maternal weight: 15 st. 11 lb. (100.2 kg.). The weights both of the mother and of the infants were probably significant in this case.

Case 10.—Patient aged 24. *First pregnancy:* emergency admission on February 4, 1948; three weeks in an antenatal ward; B.P., 220/140; scanty secretion of urine; alb., 20 parts; granular and hyaline casts; blood urea, 60 mg. per 100 ml.; headache; epigastric pain; vomiting. Eyes: slight retinal oedema and evidence of hypertension in arteriovenous crossings. February 24: caesarean section; male infant, 3 lb. (1.4 kg.); died on fourth day. Alb., 0.5 part, present in urine when she left hospital. *Second pregnancy:* E.D.D., January 14, 1949. Hypertension at 28 weeks; admitted. Maternal weight, 8 st. 2 lb. to 9 st. 8 lb. (51.7 to 60.8 kg.); B.P., 140/80 at six weeks; 140/76–155/95 in ward; no proteinuria. Eyes: fundi satisfactory. January 23: female infant, 5 lb. 5 oz. (2.5 kg.); did well. December 21, 1949: B.P., 140/80; neither protein nor abnormal cells discovered in urine.

Discussion of Results

I recounted the obstetric history of the second "denervation" patient, while she was still pregnant, to a colleague whose opinion is valued very highly throughout the country and asked him what chance he thought she had of a living child. He replied that her only sporting chance was a caesarean section at about the 34th week of pregnancy. She delivered herself of a healthy infant weighing 7 lb. 8 oz. (3.4 kg.), at the 38th week, after a completely uneventful pregnancy. In my judgment it is most improbable that any of these three patients could have given birth to a living child, and the fact that each of the three has a healthy infant can reasonably be attributed to the operation that was performed.

It is nevertheless necessary to exercise the utmost caution in accepting any such conclusion, and for this reason all the known relevant cases, occurring among some 30,000 deliveries during the past five years in Bradford, have been reviewed. It will be seen that four patients who developed the pre-eclamptic symptomatology at or about the 30th week of their first pregnancies did have normal second confinements. A further five such patients were delivered of healthy children at term, although the pregnancy in each case was complicated by hypertension and in three cases by proteinuria. It must also be recognized that hypertension, proteinuria, oedema, and other symptoms associated with pre-eclampsia do not have the same significance when occurring concomitantly with some forms of antepartum haemorrhage. A patient was recently delivered of a perfectly healthy infant after a normal pregnancy. Her first pregnancy was uneventful, but her second was complicated

at the 28th week by toxaemic accidental haemorrhage, associated with B.P. 160/120 mm. Hg, alb. 14 parts, and epigastric pain. A stillborn foetus, 1 lb. 15 oz. (0.88 kg.), was delivered by caesarean section because of placenta praevia.

It is therefore my view that this operation, which is not without some risk, should not be performed until after the woman has passed through a second pregnancy during which she has received the most scrupulous care and adequate nutrition. If the pre-eclamptic symptomatology recurs and she again gives birth to a stillborn infant the internal iliac vessels should be denervated. The main disadvantage accruing from this course is that many women, and more husbands (and doctors), feel that after a second such disaster sterilization is indicated. The only exception I would make to this rule is if fulminating symptoms occur before the 26th week of pregnancy, particularly in elderly women. It is because no individual, no matter how great the amount of clinical material he sees, is likely to encounter many patients who would benefit from this operation that I have ventured to publish so small a series of cases. Experience obtained in other centres may not only lead to happiness in barren homes but may shed further light on the aetiology of eclampsia.

A few clinical points may be mentioned. All the women were reasonably healthy in the non-pregnant state, except for some slight degree of hypertension, and such tests as were carried out revealed no abnormality of renal function. Recurrent pre-eclampsia occurring at or about the 30th week of pregnancy cannot reasonably be attributed to abnormal afferent impulses arising in an overdistended uterus, particularly as the foetus is usually unduly small. A study of the cases reported does not reveal that any sudden or great increase in weight characterized more than two of the pregnancies. Case A, the first of the denervation cases, put on only 5 lb. (2.3 kg.) in the seven weeks of her second pregnancy, during which the pre-eclamptic syndrome developed. She put on over 2 st. (12.7 kg.) in her successful third pregnancy. Case C did increase her weight by 22 lb. (10 kg.) between the 14th and the 22nd week of her first pregnancy, but she lost 9 lb. (4 kg.) during the next fortnight.

It is generally agreed that the above symptomatology is often associated with a scanty secretion of urine, but this is not always the case. Case C, who possessed only one kidney, passed urine very freely throughout her stay in the antenatal ward, and actually passed 205 oz. (5,825 ml.) in a 24-hour period. At that time the changes in her retinae were marked.

Nutrition of the Placenta

It might be conjectured that imperfect nutrition of the placenta, particularly in those critical weeks while it is being formed, might result in: (*a*) premature birth of the foetus; (*b*) certain foetal malformations; (*c*) death of the foetus, without any maternal toxaemic symptoms; (*d*) death of the foetus associated with ante-partum haemorrhage and certain types of accidental haemorrhage; and (*e*) pre-eclampsia and eclampsia, with or without death of the foetus.

The imperfect nutrition of the placenta might be either qualitative or quantitative, the former defect being due to imperfect nutrition of the mother and the latter to the deficient volume of blood which reaches the placenta. This volume is determined by the actual cross-sections of the arteries concerned, which could theoretically be reduced by spasm. The internal iliac arteries were very noticeably reduced in size in two of the patients operated on, and in one were not much larger in diameter than the radial artery. It has already been mentioned that Bartels (1928) and Wettley (1938) reported that a hypoplastic vascular system was often associated with eclampsia.

Such speculation is attractive and would not appear to be contradicted by known facts. It must, however, be borne in mind that the number of pregnancies which cannot be brought to a successful conclusion by thorough antenatal care is extremely small. Further, even if it be assumed that occasional cases are encountered in which the blood supply to the placenta is so limited by the actual size of the arteries directly or indirectly supplying the uterus that the pre-eclamptic syndrome invariably supervenes, it by no means follows that pre-eclampsia and eclampsia can invariably be attributed, either in part or in whole, to imperfect nutrition of the placenta. As well might it be argued that blindness is invariably due to opacities in the cornea.

Significance of Afferent Nervous Impulses Arising in the Uterus

It may be assumed that any increased blood supply afforded to the placenta was effected through the division of efferent nerves which constricted the internal iliac arteries. No evidence was obtained to show that afferent fibres arising in the uterus play any part in the pre-eclamptic symptomatology. Considerable distension of the post-partum uterus with a rubber balloon filled with water exerted no effect either on the blood pressure or on water diuresis; neither did a faradic current delivered to the cervix by means of a twin electrode. These experiments were, however, of short duration, and the possibility that prolonged stimulation of these nerves might interfere with the secretion of urine cannot be excluded.

Painting the lower portions of the abdominal aorta and inferior vena cava, the internal iliac vessels, and the ureter on the left side with a 5% solution of phenol, together with the destruction of the lower part of the lumbar sympathetic chain, caused no measurable alleviation of symptoms in a pre-eclamptic patient, although the pregnancy was allowed to continue for six weeks after the operation. The foetus did survive, although it did not increase much in size. Bayliss and other physiologists have used this strength of phenol solution for the destruction of sympathetic nerve fibres, and Doppler (1925) introduced the method into surgery. It may be supposed that many nerve fibres were destroyed, but neither the increase of blood supply afforded to the placenta at this stage nor the cutting off of afferent impulses served to ameliorate the pre-eclamptic symptomatology. It is of interest to note that the wide destruction of pelvic sympathetic nerves, combined with presacral neurectomy, caused no obvious diminution of the pains of labour.

Conclusion

It is suggested that denervation of the internal iliac vessels is a justifiable and worth-while procedure in women who have twice suffered from pre-eclampsia, associated with death of the foetus, at or about the 30th week of pregnancy. It is possible that denervation of the internal iliac artery on either side will suffice, without stripping the veins, and if this be the case the operation will be shorn of its main danger and could be advocated more freely. Presacral neurectomy was not performed in the first successful case and is most likely unnecessary. These and other cases provide no justification for the assumption that prolonged hypertension and proteinuria occurring during pregnancy cause either chronic nephritis or hypertension.

Summary

A woman in whom the eclamptic syndrome does not manifest itself before the 38th week of her first pregnancy almost invariably has subsequent normal pregnancies.

If, however, the pre-eclamptic syndrome occurs at or about the 30th week of pregnancy, notwithstanding adequate antenatal care, the same symptomatology is likely to recur in subsequent pregnancies and to manifest itself at about the same period of gestation. The foetus, moreover, is likely to be very small.

Three successful pregnancies subsequent to denervation of the internal iliac vessels are reported. The first patient had had two stillbirths and the second three stillbirths. The third patient had had a fulminating attack of pre-eclampsia at the 22nd week of her first pregnancy and possessed but one kidney.

It is suggested that adequate nutrition of the placenta, particularly when it is being formed, is essential to a normal pregnancy, and that in a very few cases the actual size of the internal iliac arteries makes this impossible in the presence of normal arterial tone.

The fact that adequate nutrition of the placenta is essential to a normal pregnancy by no means excludes the necessity for the proper nourishment of the maternal organs, and in the vast majority of cases the one requisite is impossible apart from the other.

No evidence was obtained to suggest that the pre-eclamptic syndrome can be attributed to afferent nerve impulses arising in the uterus.

The cases studied provide no support for the view that long-sustained hypertension and proteinuria during pregnancy cause either chronic nephritis or hypertension, or can be attributed to a "renal shunt."

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THE PSYCHIATRIST AND COMPENSATION NEUROSES*

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The term "neurosis" as used in litigation is notorious for the looseness of its application. It is in fact a term which is applied generally to describe any mental disorder, short of an obvious psychosis, following an injury.

As a preliminary, therefore, to any discussion on the question of compensation neuroses, I think it advisable to refer to the various types of mental disorder which are associated with trauma. The obvious psychotic results of brain-tissue damage from direct injury vary from the acute traumatic deliria to mental defect. The post-traumatic constitution of Adolf Meyer and the post-concussional or contusional states of Henderson may appear obscure to the general practitioner or to the lawyer but are none the less definite morbid conditions of grave significance, undoubtedly brought about by tissue damage. They have a reasonably objective symptomatology, and in many cases have a positive electroencephalographic reading. The psychoses, which are less obviously associated with direct brain injury, include the various well-recognized constitutional syndromes of schizophrenia, manic or depressive states, and paranoia. The attributability of these constitutional syndromes to injury, either with or without head injury, depends very largely on the factor of coincidence—namely, the development of the psychosis in a previously normal person within a reasonable time after the injury. The fact that there may have been evidence of cerebral damage, such as amnesia or other confusional signs, is not in itself complete assurance that the injury was responsible for the development of the psychotic state. It is merely corroborative of the supposition based on the chronology of evidence that the psychosis was precipitated by the injury.

To come to the question of so-called compensation neuroses, it is a first essential to define as accurately as possible the meaning of neurosis. It may be said at once that, except in so far as neuroses associated with injury involve the question of compensation, there is no such entity as a compensation neurosis. Such an appellation might be applied with equal justification to more obvious results of injury—for example, compensation fracture, dislocations, etc.

The neuroses which follow an injury do not in any way differ symptomatologically or otherwise from the neuroses met with daily in psychiatric clinics, where no question of compensation arises, but merely the question of treatment. They are well-defined syndromes of varying degrees of severity, and, while there may be overlapping of symptoms complicating the diagnosis, they have been classified under well-recognized headings of neurasthenia, anxiety states, obsessional states, and hysteria.

Henderson, in his textbook of psychiatry, makes a distinction between traumatic neuroses and traumatic psychoneuroses, attributing the former to physical damage and the latter to the psychological effect on the personality. Most authors agree that the extent or site of the injury has no specific bearing on the nature or type of the neurosis. This has been conclusively shown in the studies of the neuroses occurring in large groups during the war.

The work of Parfitt on neuroses in the R.A.F., of Guttman and Baker on neuroses in firemen during the war, and of Linford Rees on neuroses in women in auxiliary services all point to the same conclusion, that the primary aetiological factor in all cases of neurosis is a psychological predisposition, which may become manifest only when exposed to certain forms of stress. The term "neurosis of psychoneurosis" must therefore be taken as one and the same thing, with the same aetiological mechanism.

Malingering

In the approach to a case of alleged neurosis in which compensation is involved, the first essential is to make a reasonably accurate diagnosis of the nature of the neurosis, and the examining physician should endeavour to satisfy himself whether he is dealing with one of the accepted well-recognized and well-defined forms. When he has concluded his investigations he should be able to state whether the case comes under the heading of a neurasthenia, an anxiety state, an anxiety hysteria, a hysteria, or an obsessional neurosis. If he has succeeded in making a diagnosis under any of these categories he must then satisfy himself that the signs and symptoms on which he has based his opinion are not simulated. To rule out simulation is not always an easy task. The malingerer can be very cunning, as the prize is great. Malingering can be ruled out only by the careful correlation of signs and symptoms by a

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psychiatrist of great experience. The symptomatology of the neurosis is so protean in character that even a very experienced psychiatrist may be unable to arrive at a definite decision in certain cases, and wrong judgments have been made on that account, but at least the margin of error is reduced to a minimum by such a scientific approach. Accuracy in defining the nature of the neurosis is one of the surest methods of obviating malingering.

Attributability

In cases of neuroses alleged to have been brought about by injury and in which compensation is involved the question of attributability is the first important consideration. It is well to consider what are the accepted theories of aetiology. These theories, as already pointed out, all agree that the neuroses are mainly psychogenic, that they are a dysfunction of the mental processes brought about by subconscious motives. Freud expounds that they are all degrees of the same process—namely, anxiety—and that obsessions and hysterical manifestations are purely symptoms or symbols of varying degrees of anxiety. The results of psycho-analysis support this theory.

While neuroses may occur without any external cause, the great majority may be shown to have precipitating factors, either of continuous nature in the environment or of a dramatic nature. It is the first objective of the examining psychiatrist, in any case, to endeavour to ascertain what are the contributory or precipitating factors. These factors may be found in the simple economic, social, or sexual problems of life, or may consist of emotional stress of a dramatic nature, such as a harrowing experience—a young person exposed to scenes of revulsion or to an assault. Infective or toxic processes may be precipitating factors.

The conclusion to be drawn is that in certain individuals, if bodily and nervous tension is lowered by psychological or physical processes, a neurosis may develop as a result. Such individuals must be regarded as possessing what has been labelled predisposition to neurosis.

Predisposition

What is predisposition to neurosis? As a vernacular term it merely means that a state of neuroticism exists, hitherto kept in check but now coming to the surface owing to release of normal control. Such a conception of predisposition carries the implication that the individual was never really normal and previously had only the outward appearances or normality, and that, in fact, the neurosis must become overt in any case at some time. If this conception were to be accepted by judicial authorities the attributability of neurosis to injury would be regarded as very small indeed and compensation would be measured not in terms of the gravity of the neurosis but in terms of the very small part which the injury would be expected to play as a contributory factor. As it is correct to assume that all cases of neurosis which occur after the traumatic episode must have had a predisposition, the understanding of the meaning of predisposition is very important.

Predisposition, which has been defined as a "want of harmony or a state of functional weakness in some organ," is one of the most important factors not only in mental illness but in organic illness. The basis of all pathology depends on it. It consists in a hidden morbid reactive tendency in the organism which can reveal itself only under certain conditions. In the field of organic pathology science has not been content to accept complacently predisposition towards disease as an indication of an insurmountable defect but rather to regard it as an incentive to examine, analyse, and combat the pathology which renders one organism more prone than another to be affected by pathogenic conditions. The fact that only a small percentage of a group of people exposed to any type of infectious disease develop that disease is proof that predisposition towards the disease exists in a certain number. That predisposition may be due to many different causes. It may be a congenital lack of resisting qualities; it may be the failure to develop an immunity in early life; it may be an acquired defect from dietetic reasons, etc.

In mental illness, predisposition may depend on maldevelopment of particular cerebral organs with hypofunction of any organ such as the digestive, renal, or genital glands; it may be dependent on a disorder of metabolism; it may be the result of alcohol intake or toxic processes; it may be the conditioning of the organisms in the formative years or merely a faulty adjustment at critical stages of development. It must be regarded as a susceptibility to disease which under normal conditions may remain hidden in the adult but be revealed under the influence of particular morbid agents or when subjected to some exceptional strain. The quality or quantity of the strain is unpredictable and can be assessed only when the effects have become apparent. Predisposition, then, may not be referred to as a condition which would lessen the responsibility of the precipitating factor, such as injury, direct or indirect, in causing a neurosis.

Prognosis

Of equal importance to assessing attributability for neurosis to injury is the estimation of prognosis. The neuroses vary in their incapacitating effect. A large number of the various types of neuroses do not result in incapacity to pursue normal avocations. Apart from the painful preoccupation with the anxiety, obsessional, or hysterical state, the necessities of reality are observed and carried out, and patients who are capable of carrying on their normal occupations have a reasonably good prognosis of recovering from even the painful effect. Every psychiatrist in practice has a large group of people suffering from these mild neuroses who come at intervals for reassurance and advice. It is conceivable that if such patients felt that their neuroses were brought about by an injury for which they could get compensation they would not make the required effort to occupy themselves, as it is only necessity which compels them to do so.

It is such mild cases that are responsible for the prevalent idea that all cases of traumatic neuroses recover when their compensation is settled. Practically all the reliable literature on this question goes to show that settlement of the compensation does not result in recovery except in a small percentage. This small percentage consists of the very mild cases.

I do not distinguish any difference between the prognosis of graver cases of neuroses attributable to injury than similar cases in which injury is not a factor. It is determined to a large extent by the question of treatment. Most cases of anxiety neurosis will respond to energetic modern scientific treatment if available. Obsessional states and hysterias are more intractable to treatment, largely on account of the fact that the psychotherapeutic treatment which is in each individual case necessary is of such prolonged nature, and also because the standards of psychotherapeutic treatment vary very much. I think it reasonable to say that the facilities for such prolonged psychotherapeutic treatment in individual cases up to now were so short of requirement that a false attitude of pessimism with regard to the outcome of these graver types of neuroses has been generally accepted. Such standards, however, have to be taken into account, and it has to be admitted, therefore, that the hope of recovery for a considerable portion of these neuroses is poor, and that the opinion so generally expounded that most traumatic neuroses get well when the compensation has been settled is not correct.

Legal Procedure

The system of judging medical evidence in courts of law has been the subject of various deprecatory references, mainly by members of the medical profession. The principal arguments put forward against the present system are: (1) The atmosphere of opposition, inherent in a court, is apt to encourage the formation of a bias which may

unwittingly influence the opinion of some doctors. (2) That the effort to discredit medical evidence by counsel in cross-examination may confuse a medical witness not experienced in courts of law, and distort the reasons on which he bases his opinion. (3) That the conflict of opinions expressed by doctors in courts serves to bring the medical profession into disrepute. (4) That the references to which a doctor can point in support of his opinion are so limited by legal requirements of evidence that a sound opinion may appear to lack a proper basis.

While these objections have a certain amount of justification it must be admitted that opinions expressed by doctors often differ very widely, and it would seem that where different opinions are put forward medical evidence can be assessed only by the recognized methods of examination and cross-examination in order to arrive at the truth. The difficulties met with in assessing medical evidence have been recognized by legislation, which under the Workmen's Compensation Act provides for a medical referee. The Workmen's Compensation Act also provides that the medical referee may enlist the services of a specialist. It is common knowledge, however, that these provisions are not availed of fully by the courts, and in cases in which mental illness is at issue it is practically unknown that the courts employ an independent psychiatrist to assist the judge. It should be very apparent that only a person highly trained in psychology and mental illness is capable of following the anamnesis on which the diagnosis and prognosis are based. It would seem, therefore, that when mental illness is a matter of litigation it would be a good thing if the courts had a psychiatrist of well-recognized experience and standing to help in assessing mental illness in such cases, as it must be extremely difficult, if not impossible, for a judge to distinguish between the various points on which conflicting opinions are based.

Summary

There is no medical entity called a compensation neurosis. So-called compensation neuroses do not differ from neuroses in which only the desire for treatment is involved.

It is essential, in dealing with an alleged case of neurosis, to make as accurate a diagnosis of the illness as possible—whether neurasthenia, obsessional or anxiety state, or hysteria—and to assess the contributory or precipitating agents.

Accurate assessment of the nature of the neurosis is one of the best guards against malingering.

Predisposition is one of the most important factors in mental illness, and consists in a susceptibility to disease which remains latent under normal conditions but may be activated by exceptional stress.

Only the very mild cases and malingerers recover after settlement of compensation claims; the more serious cases are not affected.

Medical witnesses often differ in their opinions of cases, and judge or jury should not have to decide between them. Delicate decisions that have to be made by the court should be based on the advice of a properly constituted panel of specialists in neuropsychology.

The Lasdon Foundation Inc. has made a grant of $15,000 to Harvard Medical School and the Peter Bent Brigham Hospital to support research on the homologous transplantation of human and animal kidneys. The work will be under the direction of Professor G. W. Thorn and Dr. B. F. Miller. In previous investigations on this subject at Harvard the kidney has been transplanted into the subject's thigh and attached to the vessels of the leg. The Harvard workers hope that their studies will also throw light on the related problems of the homologous transplantation of skin and endocrine tissue.

CLOSTRIDIAL MYOSITIS ASSOCIATED WITH INJECTIONS OF SODIUM SULPHATHIAZOLE

BY

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Of the many papers which record the occurrence of gas-gangrene as a complication of drug injection in man we have examined 39, published between 1931 and 1950, but find no reference to the occurrence of this infection at the site of injections of sulphonamide. The case presented here is that of clostridial myositis associated with injections of sodium sulphathiazole.

Clinical Record

A married man aged 54, a butcher and gardener by occupation, was admitted on May 12, 1950, from the casualty department to the medical ward for the treatment of bronchitis. There was a history of angina pectoris of some eight years' standing, and he had been in the habit of drinking six to ten pints (3.4 to 5.7 litres) of beer daily.

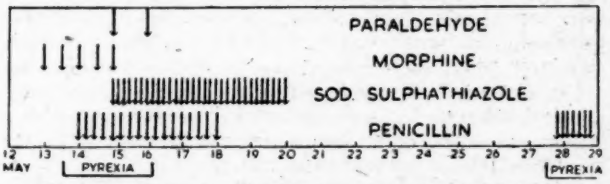

Diagram of events. Each arrow represents an injection.

The day after admission he had a severe haematemesis followed by collapse, for which morphine, ¼ gr. (11 mg.), was injected, and eight pints (4.5 litres) of compatible blood was transfused during the subsequent twenty-four hours. On May 14 his temperature rose to 102.8° F. (39.3° C.), early bronchopneumonia was diagnosed, and intramuscular injections of penicillin were begun, 200,000 units being given at intervals of six hours. The pyrexia was maintained during the next day, and intramuscular injections of sodium sulphathiazole were begun, the first of 2 g., then subsequent four-hourly injections, each of 1 g., as a 33.3% solution in apyrogenic sterile distilled water; injections of penicillin and sulphathiazole were made into the lateral thigh muscles. Administration of morphine was stopped on this day, a total of five injections, each of ¼ gr., having been given into the arms and the first of two intramuscular injections of paraldehyde, 5 minims (0.3 ml.), was administered. There is no record of the site of injection of the paraldehyde.

The temperature fell to normal on May 16; penicillin was discontinued on the 18th, when a total of 3,400,000 units had been injected; and on the 20th the injections of sulphathiazole were stopped, a total of 32 g. having been administered intramuscularly.

There was steady clinical improvement until May 28, eight days after the last injection, when the temperature rose sharply from normal to 103.2° F. (39.5° C.), the right thigh became uniformly swollen and hot, and an effusion developed into the right knee-joint. The condition was thought to be femoral thrombosis or a deep abscess in the thigh, and four-hourly injections of penicillin, each of 200,000 units, were begun.

No improvement in the general or local conditions occurred, and in the early morning of May 29 the patient woke up, complained of pain in the chest, gave three gasping respirations, and died.

The above diagram illustrates the sequence and timing of events.

Post-mortem Findings

The post-mortem examination was conducted thirty-two hours after death, the body having been stored at about 4° C. Externally the body appeared well nourished, there was some pallor of the lips and nail-beds, and the livid markings were light pink in colour. Needle-puncture marks were seen on the lateral aspect of each thigh, the right thigh was swollen, and the right knee-joint was enlarged by effusion. The skin of this region was tense and discoloured by patchy blue and pink markings, and there was "marbling" due to prominence of the superficial veins. The left thigh appeared normal in size and colour. The scrotum was red and oedematous. Incisions into the right thigh revealed widespread necrosis with liquefaction and gas production in the lateral group of muscles deep to the injection marks in the skin, the appearances being typical of clostridial myositis. Similar changes, but without gas production, were found in the right psoas and iliacus muscles. Several localized areas of coagulative necrosis, each deep to an injection puncture in the skin, were found in the lateral muscles of the left thigh; no necrosis of the superficial fat was present, and each necrotic area lay deeply in muscle. There was no evidence of infection in this thigh.

Considerable haemolysis was present in the general circulation, with staining of the blood vessels. Little aortic atheroma was found, but a solitary plaque was demonstrated in the upper part of the anterior descending branch of the left coronary artery, immediately below which was a recent ante-mortem occluding thrombus. No evidence of gas embolism could be demonstrated in any part of the circulatory system.

Chronic bronchitis was found, and a partially healed acute gastric erosion was seen on the posterior wall of the cardiac end of the stomach; no free blood was present. The liver was slightly enlarged by fatty change and discoloured by haemolysis. The spleen was slightly enlarged, dark red in colour, and congested. Blood-stained urine was present in the bladder. The brain was oedematous, a few cerebral petechial haemorrhages were seen, and there was blood-staining of the cerebrospinal fluid.

Microscopy.—Histological examination confirmed gas-gangrene of the muscles of the right thigh, and many Gram-positive bacilli were seen in sections. Neither clostridial lesions nor organisms were found in sections of the liver and other viscera, and the necrotic masses in the left thigh were also free from any infection.

Bacteriology.—A direct smear from the necrotic muscle of the right thigh showed pus cells and Gram-positive bacilli. Anaerobic cultures produced a heavy pure growth of *Clostridium welchii*, while aerobic cultures remained sterile. No organisms were cultured, either by aerobic or by anaerobic means, from the brain and cerebrospinal fluid or urine, and only coliform bacilli were grown from the spleen. The *Cl. welchii* was found to be resistant to penicillin and sulphonamides. Efforts to trace the source of the infection were unsuccessful. Suitable cultures were attempted from ampoules of sulphathiazole, apyrogenic distilled water, and paraldehyde, each from the same batch as that injected in this case. Scrapings from the two ward sterilizers were cultured, and the surgical spirit was similarly investigated, but no clostridia were grown.

Experimental Investigations

The *p*H of the sodium sulphathiazole, when made up as a 33.3% solution in sterile distilled water, is about 10.5, and it was thought desirable to investigate the growth of *Cl. welchii* in alkaline media. This investigation was deferred because of extensive structural laboratory alterations, and the original strain of *Cl. welchii* was inadvertently destroyed during the delay; subsequently three further strains of *Cl. welchii* were used.

Tubes containing 0.1% glucose broth, set up to cover a *p*H range of 10.5 to 4 by adding varying quantities of concentrated sulphuric acid and concentrated sodium hydroxide, were inoculated with the clostridia. No growth occurred at *p*H 10 and higher or at *p*H 6 and lower, and the latter observation was confirmed on repeating the experiment from *p*H 7 and below.

In order to avoid precipitation of calcium from the media, two further experiments were performed; in the one concentrated hydrochloric acid and in the other glacial acetic acid was substituted for sulphuric acid. As growth had been shown to occur on the alkaline side of neutrality, only tubes with *p*H values of 7 and below were set up. No growth occurred at *p*H 6 and below with hydrochloric acid, or at *p*H 5.5 and below with acetic acid. The tubes in which no growth occurred were reinoculated and further incubated, but again there was no growth (see Table).

Effect of pH on Growth of Cl. welchii in 0.1% Glucose Broth

*p*H	Conc. H_2SO_4 and Conc. NaOH	Repeat with Conc. H_2SO_4	Conc. HCl	Glacial Acetic Acid
10·5	−			
10·0	−			
9·5	+			
9·0	+			
8·5	+			
8·0	+			
7·5	+			
7·0	+	+	+	+
6·5	+	+	+	+
6·0	−	−	−	+
5·5	−	−	−	−
5·0	−	−	−	−
4·5	−	−	−	−
4·0	−	−	−	−

+ = Growth. − = No growth.

It thus appeared that the inhibition of growth was related to the acidity and not to calcium precipitation. We have since found references to the effect of *p*H on the growth of *Cl. welchi*, in which it is shown that this organism is cultured only with difficulty at low *p*H values (Gale, 1941; Gale and van Heyningen, 1942).

Discussion

The depth, position, and number of the necrotic foci in the muscles of the left thigh indicate the sodium sulphathiazole as the necrotizing agent in this case, and as injections of the compound were given into each thigh it is reasonable to suppose that similar necrotic lesions had been present in the right thigh, later becoming unrecognizable when the myositis developed. We have seen identical foci of muscle necrosis due to sodium sulphathiazole injections in other cases, and similar lesions are mentioned in the literature (Banks, 1940; Selbie and McIntosh, 1943). The necrosis seems to be due to the very alkaline reaction of the injection solution.

It is well known that deep necrosis of muscle is a favourable site for infection by clostridia, and the local *p*H in this case would have been above 7.7, though reduced from the initial high *p*H of the solution by buffering in the tissues and by dilution by oedema. There can be little doubt that the infection began in a sulphathiazole-induced necrotic focus in the right thigh: the organism isolated from the muscle happened to be resistant *in vitro* to penicillin and to sodium sulphathiazole; but, even had *in vivo* sensitivity to the latter been a characteristic of the bacillus, infection could still have occurred, as dormant spores might well have persisted in the tissues until the effective concentration of the sulphonamide became reduced, when active infection of the necrotic muscle would occur.

It has been shown that if an injection of *Cl. welchii* into the thigh muscles of mice is followed one hour later by injection of sulphathiazole into the same site, then only a small percentage of the mice survived (McIntosh and Selbie, 1943).

The source of the *Cl. welchii* in this case was not discovered: skin contamination from the bowel is a possibility,

the organism being a normal inhabitant of the intestinal tract of man. The customary brief skin "cleansing" with alcohol would not be sufficient to kill spores. Alternatively, the organism may have been present in any of the injection solutions or apparatus; proof of this is impossible to obtain.

Summary

Myositis due to *Clostridium welchii* infection was found in the region of injections of sodium sulphathiazole at the post-mortem examination of a man who died of acute coronary thrombosis. It is believed that the very alkaline solution of sulphathiazole was responsible for muscle necrosis, and that accidentally introduced infection of a necrotic focus led to gas-gangrene. The possible source of the infection is mentioned, and some simple experiments in the culture of *Cl. welchii* at varying *p*H values are described

We are grateful to Professor H. W. C. Vines for valuable advice and to Mr. H. Neville Stafford, coroner for Westminster, for permission to publish.

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PETHIDINE AND THE TRIPLE RESPONSE

BY

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Zuck (1951) and Pearce (1951) observed that the intravenous injection of pethidine was followed by the appearance of a wheal extending proximally along the line of the vein. Nasmyth and Stewart (1950) observed that the injection of pethidine into human skin produced a triple response which was reduced in extent by antihistamines, and suggested that pethidine was a histamine liberator. We have made similar observations. In view of the widespread use of pethidine and reports of unexpected hypotension and collapse following its administration (Giff, 1947; Butler, 1951; Zuck, 1951), it was decided to investigate the production of this triple response further. The results are reported below.

Methods

Intradermal injections (0.1 ml.) were made into the skin of the forearm with a Mantoux syringe.

The effects of intravenous injections were studied under two different sets of conditions. (1) *Venous congestion*:—A sphygmomanometer cuff was placed round the upper forearm and pumped to 70 mm. Hg. The injection (in a volume less than 0.5 ml.) was made into a small wrist vein. Immediately the needle was removed, pressure was applied with a pad of cotton-wool over the site where the vein had been punctured to prevent blood leaking out of the vein. The pressure in the cuff was maintained for three to four minutes after the injection and then released. (2) *Circulatory occlusion*:—A sphygmomanometer cuff was placed round the upper forearm and pumped to 70 mm. Hg. This pressure was maintained for one minute to congest the vessels of the forearm and then raised to 200 mm. Hg. One minute later the injection was made into a wrist vein, and after a further five minutes the pressure was released.

The Intravenous Injection of Pethidine and Histamine

A triple response is seen over the veins in the forearm if pethidine (25–100 mg.) is injected into a wrist vein with an unrestricted circulation in the arm. The reaction is more conveniently studied if smaller doses (5–15 mg.) are used with some obstruction of the venous return as described above.

Within 30 seconds of injection under these conditions an intense sensation of itching spreads up the forearm. This is often followed by a change in the colour of the vein to a characteristic mauve or plum colour. At the same time a flare appears in the skin round the site of injection and then on each side of the vein for a distance of up to 3 cm., progressively following the vein up the forearm. Within five minutes of injection a wheal appears, localized at first to a thin strip over the vein, but later spreading a few millimetres into the skin on each side. If the vein divides, the flare and wheal follow the branches. Sometimes an unaffected area of skin is seen between the site of injection and the changes higher up in the forearm. Whealing and flaring may occur distal to the site of injection and occasionally discrete wheals form in the skin. Massive wheals are sometimes seen. The typical appearance following an injection of pethidine under these conditions is shown in Fig. 1.

Within two or three minutes of the intravenous injection of pethidine with the circulation *occluded*, a red reaction is seen in the skin. A number of discrete irregular red areas appear, some distal and some proximal to the site of injection. The areas lie over and on each side of the veins in the forearm. They increase in size slowly and may coalesce. When the circulation is re-established and the reactive hyperaemia has subsided the forearm is seen to be extensively whealed, and the margins of the wheals roughly correspond with the margins of the previously observed red reactions. Surrounding all the whealed areas there is a bright red arteriolar flare. On four occasions after the pressure in the cuff was released, the subject's face was seen to flush, and a characteristic metallic taste and a transitory headache were experienced, indistinguishable from those produced by injections of histamine.

All these changes, except the very large wheals, may be reproduced exactly if histamine (15–30 μg. in terms of the base) is substituted for pethidine in the above experiments.

The lymphatic vessels play no part in this response, as the following experiment shows: if pethidine or histamine

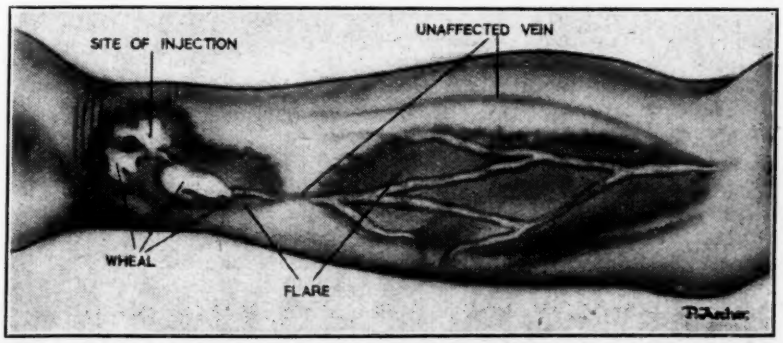

FIG. 1.—Changes in the forearm after 15 mg. of pethidine injected intravenously. Sphygmomanometer cuff (at 70 mm. Hg) at the elbow for four minutes after injection.

is injected intravenously with the veins congested, and immediately after the injection a tourniquet is applied to the forearm just proximal to the site of injection, the changes in the forearm occur in their usual sequence.

These observations can be most readily interpreted by assuming that the vein wall is permeable to both histamine and pethidine.

Effect of "Histamine Liberators" on Skin Over Vein

MacIntosh and Paton (1949) have shown that, although the injection of a histamine liberator compound into the skin is followed by a triple response, a second injection of the same substance into the same site within 24 hours produces either no response or one that is much reduced. They suggested that the original injection had reduced the normal complement of histamine in the skin, and that this had not been restored by the time the second injection was given. We have found that the skin behaves similarly after intradermal injections of pethidine (50 μg.), which supports the conclusion that pethidine is a histamine liberator.

Pethidine (10 mg.) was injected intravenously while the circulation was *occluded* and the areas of red reaction were outlined in ink. Twenty-four hours later pethidine (50 μg.) was injected intradermally into an area of skin which had previously shown a red reaction. The response was grossly reduced compared with an intradermal injection of the same amount into a comparable site on the other forearm. An intradermal injection of histamine had its usual effect. It seems likely, therefore, that the triple response seen after an intravenous injection of pethidine is due to the liberation of histamine from the skin.

Effects of Antihistamines

Treatment with an antihistamine drug modifies the triple response to a subsequent intradermal injection of histamine. Experiments were therefore carried out to investigate the results of (*a*) the oral administration of an antihistamine drug (diphenhydramine hydrochloride) on the response of the skin to an intravenous injection of pethidine given two hours later; (*b*) the injection of mepyramine alone; and (*c*) the intravenous injection of mixtures of mepyramine and pethidine and of mepyramine and histamine.

Effect of Pre-treatment with Diphenhydramine Hydrochloride (100 mg.) on Skin Response in Forearm after Intravenous Injections of Pethidine (100 mg.)

Subject	Effect of Pethidine	
	Without Diphenhydramine Hydrochloride	With Diphenhydramine Hydrochloride
1		0
2	++	
3		++
4	++	
5		+
6	++	+
7	++	
8	++	
9	++	
10		0
11		+
12	++	
13	++	
14		+
15		+
16	++	

0 = No response.
+ = Mauve vein coloration with or without flare.
++ = Includes whealing of all grades.
Subject 6 was seen twice, with three-weeks interval between observations.

(*a*) In a series of 16 cases for operation, it was arranged that half the patients received diphenhydramine hydrochloride (100 mg.) by mouth two hours before the anaesthetic was given. The patients were induced with thiopentone, and then pethidine (100 mg.) was injected into a wrist vein. The reactions in the forearm were noted and graded on a rough quantitative scale (see Table) before the observer knew which patients had received diphenhydramine hydrochloride. All except one of the subjects who received this drug showed either no changes in the skin or a much reduced response compared with the controls.

(*b*) The intradermal injection of mepyramine is followed by the appearance of a red reaction in the skin (Halpern, 1952). This reaction may be distinguished from the red reaction produced by histamine by the following characteristics: (1) the colour is a dull rather than a bright red; (2) when the red area fades there is no "speckling" at its margin; and (3) the intradermal injection of mepyramine into an arm with the circulation occluded does not give rise to a red reaction until the circulation is re-established. When mepyramine (5–10 mg.) is injected intravenously under the conditions of *venous congestion* a red reaction is seen in the forearm which is in every way similar to that described above as following the intradermal injection of mepyramine. This red reaction is distributed along the course of the veins in a manner similar to that of the triple response after injections of pethidine. If mepyramine is injected intravenously when the circulation is *occluded* no red reaction appears until the circulation is re-established. These results may best be explained by assuming that the vein wall is permeable to mepyramine.

(*c*) The intravenous injection of mixtures of mepyramine (10 mg.) and pethidine (5 mg.) or of mepyramine (10 mg.) and histamine (20 μg.) under the conditions of *venous congestion* described above produced no whealing in the forearm, but only a red reaction similar in character to that following the injection of mepyramine alone. Further, the intravenous injection of such mixtures when the circulation was occluded produced no red reaction until the circulation was re-established.

Since mepyramine does not prevent the liberation of histamine but modifies its effects by competing with it for tissue receptors (Paton and Schachter, 1951), the inhibition of the triple response in the above experiments supports the conclusion that the vein wall is permeable to mepyramine.

Effects of Pethidine on Cat's Blood Pressure

The effects of pethidine on the cat's blood pressure were found to be substantially the same as those described by Duguid and Heathcote (1940). The fall in blood pressure in cats under chloralose following the intravenous injection of pethidine (3 mg./kg.) lasted from 45 to 90 minutes (Fig. 2). Recovery from the hypotension from pethidine was not hastened by mepyramine (0.8–1.6 mg./kg.), nor did pre-treatment with mepyramine in doses up to 3 mg./kg. modify the blood-pressure response.

It follows that the hypotensive effects of pethidine in the cat cannot be explained solely on the basis of histamine liberation.

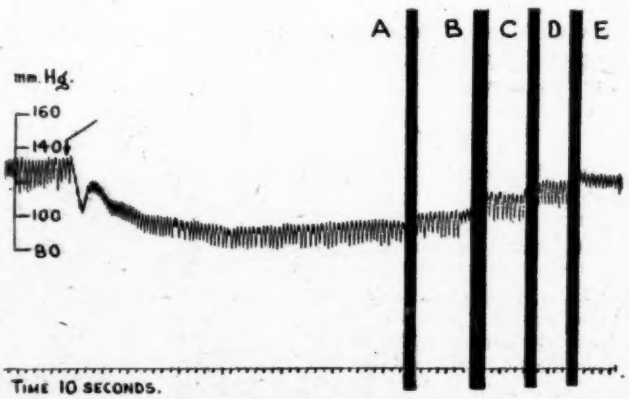

FIG. 2.—Cat, 2.9 kg.; under chloralose. Effects of pethidine (3 mg./kg.) on the blood pressure. Time of injection marked with an arrow. B, C, D, and E are successive tracings at 15-minute intervals.

Discussion

Lewis (1927) presented evidence that when a substance, other than histamine, was injected into human skin and produced a triple response, it did so by virtue of the liberation of the histamine already present in the skin but held in an inactive form. The demonstration that a triple response is inhibited by treatment with one of the antihistamine drugs supports Lewis's conclusions. MacIntosh and Paton's (1949) observations in man that the second of two injections of a histamine-liberating compound into the same site within 24 hours fails to produce a full triple response, coupled with the work of Feldberg and Talesnik (1952) on the slow rate of recovery of skin histamine following its liberation in animals, also supports Lewis's hypothesis. It follows that if any substance (1) produces a triple response on intradermal injection in man, (2) produces a reduced triple response when the subject is treated with an antihistamine drug, and (3) fails to produce the same response when a second injection is made into the same site within 24 hours, it is likely that the substance is a histamine liberator.

The present observations show that pethidine fulfils these criteria, and so support the conclusions of Nasmyth and Stewart (1950). They also provide an explanation for the observations of Zuck (1951) and Pearce (1951), and show that the walls of the veins in the forearm are permeable to pethidine, histamine, and mepyramine. No other reference has been found to the passage of substances through the walls of veins of comparable size apart from the observation of Magendie, who in the early part of the nineteenth century applied a " spirituous extract of nux vomica " to the outside of the jugular vein of a dog and observed signs of poisoning within four minutes (Franklin, 1937).

In man, the present observations show that the appearance of a triple response in the skin after the intravenous injection of pethidine is to be expected if the injection is made into a superficial vein. Although a fall in blood pressure is common after giving pethidine intravenously (Branwood, 1943), sustained hypotension and collapse are rare. The experiments on the cat indicate that, at least in this animal, the hypotensive effect of pethidine is not due solely to the liberation of histamine. It seems likely that in man some factor other than histamine liberation is involved in the production by pethidine of severe hypotension and collapse.

Conclusions

The triple response in the skin after an intravenous injection of pethidine is due to the permeation of pethidine through the vein wall and the liberation of histamine from the skin overlying it. The walls of the superficial veins in the forearm are also permeable to histamine and mepyramine.

It is unlikely that the occasional case of vascular collapse and marked hypotension following an injection of pethidine occurs as the result of the liberation of histamine.

We wish to thank Professor J. L. D'Silva for continued advice and encouragement. Miss P. Archer kindly drew the illustration for Fig. 1.

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THE "REFLUX" FACTOR IN ERYTHROCYTE SEDIMENTATION TESTS

BY

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The most popular methods of determining the erythrocyte sedimentation rate are those of Wintrobe and Westergren. The internal measurements of Wintrobe and Westergren sedimentation tubes are similar except that the length of the former is half that of the latter (2.5 mm. diameter; 100 and 200 mm. long). It was therefore surprising to find that the sedimentation rate of a specimen of oxalated blood determined in a Wintrobe tube differed from the determination in a half-filled Westergren tube. It was noticed that the period of aggregation before fall of the cells started was much longer in the Wintrobe than in the Westergren tube. The technique used to fill the tubes would seem to be the cause, since the columns of blood are identical qualitatively and quantitatively.

One way in which the method of filling the tubes differs is that in the Westergren method blood is drawn past the zero mark and then allowed to fall to it, so that a thin film of blood is left on the inside of the tube above the mark; whereas the Wintrobe tube is filled to the zero mark and the pipette withdrawn, leaving the inside of the tube above the mark free of film. In the first few minutes after a Westergren tube is set up there is therefore a reflux of cells and plasma on to the blood level at the zero mark as the blood adherent to the inside of the tube above the mark runs down to the meniscus. This reflux of blood is of course absent in the Wintrobe tube.

Since the presence or absence of this reflux of blood seemed to exert some effect on the sedimentation of oxalated blood, the effect of this factor on the classical Wintrobe and Westergren methods was investigated. The objects of this paper are: (1) to show that reflux of blood on to the meniscus is a factor frequently affecting the half-hour reading in the Wintrobe method of determining the E.S.R.; and (2) to demonstrate, in four cases in which the readings of the two classical methods were in disagreement, that if reflux of blood on to the meniscus was made to occur in the Wintrobe tube the discrepancy disappeared.

Methods

Comparisons between the readings of the standard Wintrobe and Westergren methods were made on blood from 40 unselected patients. By the Westergren method 7 showed a sedimentation rate between 0 and 10 mm., 14 between 10 and 30 mm., and 19 over 30 mm.

In four cases there was disagreement between the one-hour readings of the two methods, a raised Westergren reading being associated with a normal Wintrobe reading. Each of these patients had active organic disease, and a raised E.S.R. was expected. Blood from these four cases, and from a further 24 in which the readings of the methods were in agreement, was examined to determine the effect of reflux of blood on to the meniscus in each of the two techniques.

In the group of 24 patients in whom the standard methods gave similar readings two pairs of tubes were set up: (1) a pair of Wintrobe tubes (containing oxalated blood), and (2) a pair of Westergren tubes (containing citrated blood). In one of each pair reflux of blood on to the meniscus was allowed, in the other prevented.

Reflux of blood normally occurs when a Westergren tube is filled—in this series the blood was drawn 4 to 5 cm. past the mark and allowed to fall to it. In the tubes in which it was desired to prevent reflux the rubber tube from a W.B.C. pipette was attached to the top of the Westergren tube. Blood was sucked slowly up, and when it reached the mark was stopped by pressing the rubber tube on to the top of the Westergren tube.

Reflux does not normally occur when a Wintrobe tube is filled, the pipette being removed when the blood reaches the mark. When it was desired to cause reflux the tube was filled to the top (1 cm. above the mark), sucked back to the mark, and a small drop of blood left at the top of the tube as the pipette was withdrawn. This small drop runs back on to the meniscus.

In the four cases in which a discrepancy was known to exist between the one-hour readings of the classical methods three pairs of tubes were set up: (1) Westergren tubes (containing citrated blood); (2) Wintrobe tubes (containing oxalated blood); and (3) Westergren tubes filled to the 100 mark with oxalated blood. In one of each pair reflux was allowed; in the other it was prevented.

Results

Of the 24 cases in which the classical methods gave *comparable* one-hour readings, 5 showed an E.S.R. between 0 and 10 mm., 9 between 10 and 30 mm., and 10 over 30 mm.

One-hour Readings.—In each case the one-hour readings in all four tubes were comparable.

Half-hour Readings.—(*a*) *Oxalated blood*:—When the half-hour readings in the pairs of Wintrobe tubes were considered the cases seemed to fall into two groups—those with a P.C.V. above 37%, and those with a P.C.V. of 34% and below. The former group numbered 19, and in all these the half-hour reading when reflux was present was twice or more the half-hour reading when reflux was absent. There were five cases with a P.C.V. below 35%. In all these the half-hour readings in each pair were very similar. They were 31, 21 mm. (P.C.V. 34%); 1, ½ mm.; 15, 15 mm.; 13, 12 mm.; 36, 36 mm. (*b*) *Citrated blood*:—The half-hour readings in the Westergren tubes, with or without reflux, were usually very similar; the average difference was 2.5 mm. Nevertheless in five cases the readings varied in the ratio of 2:1 or more. In all these cases the P.C.V. was 46% or more; and it is interesting to note that the P.C.V. of the blood–citrate mixture would have been 37% or more. The half-hour readings in the five cases mentioned were 3, 1 mm.; 3, 1 mm.; 2, 1 mm.; 6, 3 mm.; and 17, 7 mm.

For the four cases in which the classical methods gave *dissimilar* results the details of the one-hour readings are set out in the Table.

Four Cases in Which the Classical Methods Gave Dissimilar One-hour Readings

Diagnosis	Westergren		Wintrobe		Westergren Half Filled with Oxalated Blood		P.C.V.
	R.A.	R.P.	R.A.	R.P.	R.A.	R.P.	
	mm.	mm.	mm.	mm.	mm.	mm.	%
Lung neoplasm ..	45	39	31	7	27	2	42
Bronchiectasis ..	22	19	22	12	33	2	48
Coronary thrombosis	60	58	38	10	37	16	46
Pyelonephritis ..	58	55	44	12	46	18	38

R.A.=Reflux of blood on to meniscus allowed.
R.P.=Reflux of blood on to meniscus prevented.

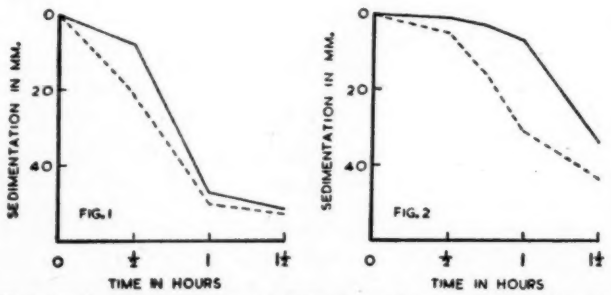
Discussion

It is clear that if the effect of a physical factor on the sedimentation rate of a blood is to be tested, the test should be made in a pair of tubes identical in every other way.

In each of the 28 cases examined a pair of Wintrobe and a pair of Westergren tubes were set up. In any pair the blood filling the tubes was identical, and they were set up in the same stand. It seems reasonable to attribute any difference between the readings of a pair to the solitary difference between them—that the one was filled so that reflux of blood on to the meniscus occurred, the other so that it was prevented.

Fig. 1 shows the usual significance of this factor on the Wintrobe method of determining sedimentation rate. The half-hour reading is considerably affected, being greater when reflux is present, whereas the one-hour reading is affected slightly or not at all. The one-hour reading in each tube agrees well with the one-hour Westergren reading.

The position was entirely different in the four cases in which the one-hour readings of the standard methods were at variance. In them (with oxalated blood), when reflux was absent, the period of aggregation before sedimentation proper starts was greatly prolonged. In each case the difference between the Wintrobe tube filled so as to produce reflux of blood and that filled without reflux, marked at half-hour, were also present at one hour. The period of "disappearance of the discrepancy" occurred between 1 and 1½ hours, instead of between the ½ and 1 hour as is usual (Fig. 2).



Variation in sedimentation rate in Wintrobe tubes (each pair filled with identical oxalated blood) according as reflux is present or absent. The continuous line shows rate without reflux, the broken line rate with reflux.

FIG. 1.—Usual pattern, with half-hour discrepancy disappearing at one hour. FIG. 2.—The pattern in four exceptional cases—the half-hour discrepancy persisting at one hour and becoming insignificant only at one and a half hours.

To corroborate that this behaviour was dependent on the method of filling the tube, and not on some inherent property of the Wintrobe tube, a pair of Westergren tubes were at the same time half filled with oxalated blood, one so that reflux of blood on to the meniscus occurred, the other so that it was prevented.

The half-filled Westergren tube and the Wintrobe tube in which reflux had been prevented gave readings of a similar order. Those with reflux present gave similar readings. The latter pair were in good agreement with the classical Westergren one-hour reading, whereas the former pair gave much smaller readings.

In all 28 cases examined reflux of blood on to the meniscus did not materially affect the one-hour Westergren reading. As mentioned above, it did affect the half-hour reading in five cases. It seems from the practical point of view that here the factor can be ignored because the Westergren tube is usually filled so that reflux of blood is inevitable, and because half-hour readings (the only ones affected) are not usually made.

The point of practical importance is that if this series of patients had been examined by someone who habitually fills the Wintrobe tube to the top and then sucks out blood to the zero mark no case would have been found in which the one-hour reading differed materially from that of the Westergren method. Whereas had the cases been examined by someone who (like myself) was accustomed to fill Wintrobe tubes to the zero mark, and then remove the pipette so that reflux of blood does not occur, four cases would have been noted in which the one-hour Wintrobe reading was at variance both with the clinical condition of the patient and with the reading of the Westergren tube.

Why the difference, described above, in the filling of the tubes should be the cause of differences in sedimentation rate in a particular blood is a question of theoretical interest. It may be due to the momentum of the cells, gained by flowing down the inside of the tube to reach the zero mark, carrying them on downwards. Their momentum might act in certain circumstances as an accelerating factor on the sedimentation of rouleaux forming near the blood surface. As other suggestions can be offered, further work is required on this problem. For the present, however, it is desired to emphasize only the practical aspects.

It seems quite clear from recent papers that there is more than one cause for discrepancy between the readings of the Wintrobe and Westergren methods. Goldberg and Conway (1952) found in two cases that the discrepancy was due to the retarding effect of the oxalate. Goldberg, Glynn, and Bywaters (1952), in a preliminary note, state that the cause of discrepancy in their cases seems to have been the effect of the anticoagulant on the blood *p*H. In both these series the discrepancy has always taken the form of a high Westergren reading with a normal or near normal Wintrobe reading. Davis (1946) has reported cases in which a high Wintrobe but normal Westergren reading has been found.

It seems that, if the Wintrobe tube is filled so that reflux of blood on to the meniscus occurs, at least one factor causing unexpectedly low Wintrobe readings will be eliminated.

Summary

The Wintrobe and Westergren readings were compared in 40 cases and found to be at variance in four, the Westergren reading being more compatible with the clinical state of the patient.

The effect of reflux of blood on to the meniscus was examined in 28 cases, including the four in which discrepancy was noted.

This factor is of no practical importance in the Westergren method.

In the Wintrobe method it affected the one-hour reading in four cases—the cases in which discrepancy was noted. In these when reflux was present the one-hour reading agreed with the Westergren reading; when it was prevented the reading was discrepant.

One of the factors sometimes causing unexpectedly low Wintrobe readings will be eliminated if the Wintrobe tube is filled so that reflux of blood on to the meniscus occurs.

Grateful acknowledgments are due to Professor Sir John McNee for providing facilities in the Gardiner Institute and for guidance in the preparation of this paper; also to Drs. H. Conway, A. Goldberg, and J. Cochran for their helpful advice and criticism.

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A note on dahlia tubers as a source of food is contributed by Mr. S. G. Harrison to the February issue of the *Journal of the Royal Horticultural Society*. The tubers consist partly of inulin, and though not palatable either to man or domestic animals they could be a useful source of laevulose if a cheap process were devised for converting the inulin into that monosaccharide. The present small demand for inulin is being partly met by a firm which is processing three tons of dahlia tubers a year to produce it; the tubers used are normal horticultural surplus. It is thought that breeding experiments might lead to the development of tubers with a higher content of inulin than the present 9% to 13%, for the sugar content of sugar beet has been increased from about 7% sucrose to about 20%.

A SURGICAL METHOD FOR MANAGEMENT OF PATIENTS WITH PORTAL CIRRHOSIS

PRELIMINARY REPORT OF A CASE

BY

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Ligation of the hepatic artery, alone or together with the splenic and left gastric arteries, has been used in recent years as a treatment for portal hypertension and its complications. Success has been claimed in a number of these cases. Ascites and bleeding oesophageal varices appear to be favourably influenced by a reduction in arterial blood supply to the liver, and liver function seems to improve.

The rational basis for this surgical method can be traced back to the studies of the intrahepatic circulation in portal cirrhosis by Kretz (1904), Herrick (1907), McIndoe (1928), and Dock (1947), and to the more recent demonstration by Montagnani and Paci (1952) of a tremendous increase in the arterial circulation in the cirrhotic liver with widespread arterio-portal shunts of varying size.

Berman *et al.* (1950, 1951) and Berman and Hull (1952) have suggested that the method works by reducing arterial blood flow and pressure in the liver parenchyma so that more blood can pass through the portal bed and portal venous pressure is lowered.

Ligation of the terminal part of the hepatic artery carried great hazard, and as a compromise the artery has been tied proximal to the origins of the gastroduodenal and right gastric branches so that a free collateral circulation is possible. Experimental studies in dogs (Montagnani, 1952) have led to the development of a method of gradual occlusion of the hepatic artery or its terminal branches by wrapping around it a "cellophane" band treated with dicetyl phosphate. This led to a fibroblastic reaction of the surrounding tissues, ending in complete obliteration of the hepatic artery. In the meantime a collateral circulation developed towards the liver through the inferior phrenic arteries and minute arterial branches along the portal vein and the common bile duct. No impairment of liver function or damage to the liver parenchyma was observed after such a procedure. No antibiotics were given at any time.

The favourable results of these experiments encouraged clinical application of the procedure in the following case.

Case Report

A man of 58 was transferred from the medical service with Laennec's hepatic cirrhosis and ascites, which had not responded to medical treatment. His father had died of hepatic cirrhosis and he himself had worked for years in a vinery, drank 1.5–2 litres of wine each day, ate little, and smoked much. For two months before admission he suffered from dyspepsia, alternating diarrhoea and constipation, asthenia, and loss of weight.

On admission he was found to be wasted and breathless. The sclerae were icteric. The abdomen was greatly distended by fluid and the lower half of the body was oedematous. Distended veins were present on the lower abdomen. There were no abnormalities in the chest. The relevant laboratory findings were: total plasma protein 5.8 g.% (albumin 2.3 g., globulin 3.5 g.); prothrombin 50%. During

two months of medical treatment the loss of weight continued and ascites recurred after repeated tapping. He was transferred to the surgical side on March 22, 1952. The laboratory findings then were: total protein 6.2 g.% (albumin 2.6 g., globulin 3.6 g.); prothrombin 50%. After treatment with vitamin K and blood transfusion, peritoneoscopy was done on April 1 to confirm the diagnosis. After further fresh blood transfusion the prothrombin rose to 65%.

Operation was performed on April 16. The abdomen was entered through a right rectus incision. About a litre of clear fluid was evacuated. The liver was small and hard, with rounded borders and grossly granular surface. The gall-bladder was small and thick-walled. The hepatoduodenal ligament was carefully dissected and the hepatic artery was found and freed. Three branches were identified: the right branch, and two smaller ones directed to the left and middle (quadrate) lobes. The portal pressure measured from an omental vein was 365 mm. of heparinized saline. After occlusion of the three hepatic branches with bulldog clamps the portal pressure fell to 254 mm. The two branches to the left and middle lobe were ligated with No. 1 linen ligatures and the larger branch to the right lobe was wrapped with two turns of a cellophane band treated with dicetyl phosphate. The arteries were buried in the hepatoduodenal ligament with three stitches of 000 silk, and the abdomen was closed without drainage.

The post-operative course was uneventful except for a haematoma of the wound followed by a small dehiscence which was repaired on May 28. The abdomen was tapped once, on May 20, to avoid the danger of a post-operative hernia, and 800 ml. of fluid was withdrawn. The patient had a normal diet from the sixth post-operative day, and by the time of his discharge from hospital on June 23 he was eating well, had normal bowel movements, and a slight amount of fluid was present in his abdomen. He had gained 1 kg. in weight.

He was seen again on September 25, when he was feeling well, had gained 5 kg. in weight since discharge, and was eating well. He had slight constipation, which he corrected with some laxatives. No jaundice was present and the venous collateral circulation on his abdomen had almost completely disappeared. He had not been tapped since his discharge from hospital, and a small amount of fluid was detectable. The plasma protein at this time was 7.39 g.% (albumin 2.97 g., and globulin 4.42 g.).

The favourable result of this first case supports the belief that the method, which was developed experimentally, is worthy of further clinical application.

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The physiology of vision is the subject of a dozen articles in the current issue of the *British Medical Bulletin*. Sir John Parsons, F.R.S., consulting surgeon to the Royal London Ophthalmic Hospital, contributes a preface which draws attention to some of the implications of modern research into vision. A mechanism that corrects the lens system of the eye so as to overcome chromatic aberration is the subject of an article by Professor H. Hartridge, F.R.S. Professor A. Sorsby discusses the nature of refractive errors, and Dr. Hugh Davson some problems of the formation and circulation of aqueous humour. In this connexion Sir John Parsons suggests in the introduction that further knowledge of the production of aqueous humour may have a bearing on the formation of cerebrospinal fluid and of lymph production in general. A useful bibliography of British books and periodicals concerned with the physiology of vision is included. The *Bulletin* is published by the British Council; the price of the current number is 15s.

TRICHLORETHYLENE IN LABOUR

BY

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Browne *et al.* (1951) described the use of Steel's inhaler for administering trichlorethylene in labour. Commenting on this, the *British Medical Journal* (1951) stated: "The argument over analgesia in labour creaks on . . . Steel's inhaler . . . unfortunately does not contain all the safeguards generally considered necessary for its use . . . by a midwife." I wish, therefore, to describe the results obtained with a "Tecota" inhaler (manufactured by Cyprane Ltd.), which contains many of these safeguards and apparently fulfils most of the specifications laid down by the Medical Research Council. The machine used is readily portable and delivers a concentration of vapour of 0.45% trichlorethylene in air with a variation of about 10% with temperature and normal breathing rates. The concentration is within these limits in all working positions and after shaking or inversion of the apparatus. The concentration falls to about 0.4% for breathing rates below a minute volume of 7 litres.

Trichlorethylene

PATIENT'S NAME..... DATE.....

TIME COMMENCED..... CERVIX.....dilated (PR/PV

TIME FINISHED.....

DURATION.....HRS.....MINS.

USED FOR BIRTH OF HEAD { YES / NO } EFFECT: Satisfactory / Unsatisfactory

BABY: First cried.....minutes after birth.

Resuscitation needed by MIDWIFE { YES / NO }

DOCTOR { YES / NO }

F. Hts..... Regular..... Irregular.....

MOTHER: Co-operation: Average Fair Poor

Ill-effects (e.g., irregular pulse, giddiness, or anaesthesia)

.....

After-effects: .....

RELIEF: Patient's opinion: Very good Good Fair Poor

Attendant's opinion:.....

.....

REMARKS: .....

.....

The investigation was instituted primarily to ascertain if the machine could be used safely by unsupervised midwives, and, secondarily, to attempt to assess its efficiency and detect its disadvantages. There are many drawbacks to such an investigation. On the one hand, the subjects are often extremely impressionable, and, on the other hand, one has to allow for the varying standards and enthusiasms of different observers. The present series of 400 cases is a personal one. All the patients were seen by me during labour and/or interviewed by me 24 hours later. The form reproduced here was completed for each patient by the supervising midwife immediately after delivery. The main points were that the administration was not begun until the cervix was dilated at least three fingerbreadths and was discontinued after six hours. The machine was charged with 30 ml. for each case and not refilled during that time. Chloral and bromide, and pethidine, were often used as premedication, but no drug was given once

the administration of trichlorethylene had begun. The results are presented on lines similar to those in the survey undertaken by the Royal College of Obstetricians and Gynaecologists (1947).

Type of Case

There was no selection of the 400 cases. Any patient who had been certified by the doctor as "fit for gas and air" was given trichlorethylene if a machine was available. The age incidence and the parity of the patients are shown in Tables I and II. Of all the hospital deliveries approximately 54% are primigravidae and 46% are multiparae. The reason

TABLE I.—*Age Groups*

Age:	20 and Under	21–25	26–30	31–35	36 and Over	Total
No.:	87 (21·75%)	138 (34·5%)	106 (26·5%)	40 (10%)	29 (7·25%)	400

TABLE II.—*Parity*

Primigravidae	1-para	2-para and Over	Total
295 (73·75%)	65 (16·25%)	40 (10%)	400

for the preponderance of primigravidae in the series is the fact that many of the multiparae were delivered so soon after admission that trichlorethylene was not given, or was used for less than the required minimum period of 20 minutes.

Efficacy of the Analgesia

The mothers were questioned immediately after delivery, and again 24 hours later; their opinions are shown in Table III. In 16 cases (4%) reflection caused the mother

TABLE III.—*Mother's Opinion of the Efficacy of the Analgesia*

Very Good	Good	Fair	Poor	Total
135 (33·75%)	155 (38·75%)	80 (20·0%)	30 (7·5%)	400

to take a more favourable view of the analgesia, and in 10 (2.5%) the reverse occurred. However, in these cases the more unfavourable opinion has been accepted for the analysis. Adequate analgesia (very good or good relief) was obtained in 290 cases (72.5%) and inadequate relief (fair and poor) in the remaining 110 (27.5%). In the observer's opinion (Table IV) adequate analgesia was obtained in 294 cases

TABLE IV.—*Observer's Opinion of the Analgesia*

Very Good	Good	Fair	Poor	Total
92 (23%)	202 (50·5%)	91 (22·75%)	15 (3·75%)	400

(73.5%) and inadequate relief in 106 (26.5%). Tables III and IV show a discrepancy in the numbers in the very good, good, and poor columns, although the combined figures for adequate and inadequate analgesia are very similar. This is probably due to the fact that the mother who has no previous experience to guide her is less likely than the trained observer to be addicted to moderation in her opinions.

In interpreting the results shown in Table V it must be remembered that many of the labours in which the administration lasted for more than four hours were in themselves long and often complicated by uterine inertia or terminated in operative delivery, factors which in themselves would lead the mothers to take a more pessimistic view of the analgesia. On the other hand, a short administration often indicated a reasonably quick labour, with the greater likelihood of a satisfactory opinion of the analgesia.

TABLE V.—*Effect of Duration of Analgesia on its Efficacy*

Period of Administration	Adequate Analgesia Very Good and Good	Inadequate Analgesia Fair and Poor	Total
Less than 2 hours	184 (75·7%)	59 (24·3%)	243
2–4 hours	76 (73·1%)	28 (26·9%)	104
More than 4 hours	34 (64·2%)	19 (35·8%)	53

Note: Cases in which trichlorethylene was administered for less than 20 minutes have been excluded from the series.

Effect of Analgesia on Course of Labour

Co-operation of Patient.—A few of the mothers refused the trichlorethylene after a few breaths. Typical comments were: "Cannot get my breath," "Instinct told me to pull it off," "Feel as if I am choking." These cases have been excluded, as the trichlorethylene was not administered for the minimum of 20 minutes. The exact number of such cases is not known, but the estimate is between 10 and 20. Apart from this, lack of co-operation occurred in two groups of cases. In the first group analgesia was excellent, but the patient became too sleepy to push during the second stage. This occurred in five cases (1.25%). The second and larger group consisted of mothers who used trichlorethylene reasonably well until the contractions became more severe late in the first stage or during the second stage, when, owing to inadequate analgesia or slow progress of the labour, they became very restless or hysterical. There were 27 such women (6.75%), in only two of whom did the observer consider that the excitable state might have been produced by the trichlorethylene.

Delay in Labour Due to the Analgesia.—The length of labour in 400 cases having trichlorethylene is compared with a similar group of 400 women the conduct of whose labours did not include the administration of trichlorethylene. These are termed "controls" (Table VI). Of the cases of uterine

TABLE VI

	Trichlorethylene		Controls	
	Primigravidae	Multiparae	Primigravidae	Multiparae
	Hrs. Mins.	Hrs. Mins.	Hrs. Mins.	Hrs. Mins.
Length of 1st stage ..	20 —	12 5	19 —	11 15
,, ,, 2nd ,, ..	1 5	— 22	— 58	— 17
Total length of labour ..	21 5	12 27	19 58	11 32

inertia it was considered that in six the trichlorethylene probably was the major factor in production of the inertia. In all these cases the administration had begun rather early in the labour.

Forceps Rate.—Forceps were used in 1 of the 105 multiparae (1%) and in 27 of the 295 primigravidae (9.2%), a total of 28 out of 400 cases (7%). The forceps rate for the hospital is 5.3%. The increase for the trichlorethylene series can be entirely accounted for by the high percentage of primigravidae in the series.

Primary Post-partum Haemorrhage.—This is defined as a loss of more than 20 oz. (570 ml.) within 24 hours of delivery. There were 12 cases (3%). The incidence of post-partum haemorrhage for the hospital, if one excludes emergencies admitted because of post-partum haemorrhage, is 3.8%.

Conclusions.—Trichlorethylene does not appear to increase the operative delivery rate or predispose to post-partum haemorrhage. Occasionally it may cause uterine inertia if begun too early in the labour.

Ill-effects on Mother

There were no maternal deaths. No ill-effects on the respiratory rate were noted. No cases of bradycardia or arrhythmia were noted, but in three cases tachycardia was possibly connected with the administration of trichlorethylene.

Conclusion.—There was no definite evidence of any ill-effect on the mother from the administration of trichlorethylene.

Effect on the Foetus

Stillbirths.—There were 10 stillbirths among the 405 babies born, a rate of 24.7 per 1,000 total births. The stillbirth rate for the hospital is 27.4.

Neonatal Deaths.—There were 14 neonatal deaths, a rate of 35.4 per 1,000 live births. The neonatal death rate for the hospital is 36.6.

Incidence of Asphyxia.—Asphyxia was regarded as present if the baby did not cry within two minutes of birth or if it required resuscitation other than clearing of the air passages. Forty cases in which caesarean section, forceps, or other operative deliveries were carried out have been excluded, as other forms of anaesthesia were used. Using the above criteria, 28 babies showed evidence of asphyxia (7.8%).

Effect of Combination of Pethidine and Trichlorethylene in Production of Asphyxia.—Of the 28 cases of asphyxia 17 (60.7%) had pethidine in addition to trichlorethylene. In the whole series 57% had pethidine in addition to trichlorethylene. Thus it seems that, contrary to the Royal College of Obstetricians and Gynaecologists report, pethidine does not increase the incidence of asphyxia.

Premedication

A potassium bromide and chloral hydrate mixture was used in the early stages of labour followed by pethidine. By so doing, adequate analgesia was provided and the administration of trichlorethylene delayed until the cervix was dilated at least three fingerbreadths. The Royal College of Midwives allows these drugs to be administered by unsupervised midwives. No other drugs were used as premedication and no analgesic was given once the administration of trichlorethylene had begun.

Of the 228 patients who were given pethidine, 163 (71.5%) were in the "adequate analgesia" group and 65 (28.5%) in the "inadequate analgesia" group. Of the 172 patients who had trichlorethylene not preceded by pethidine, 127 (73.8%) were in the "adequate analgesia" group and 45 (26.2%) in the "inadequate analgesia" group. Pethidine can safely be combined with trichlorethylene, thereby shortening the duration of the administration of the latter, though it does not appear to improve the degree of analgesia obtained.

Conclusions

Trichlorethylene administered by the method described produces satisfactory analgesia, and it can safely be combined with pethidine without increasing the risk of foetal asphyxia. It does not increase the operative delivery rate or predispose to post-partum haemorrhage. It can safely be used by unsupervised midwives trained in the method of administration, with the following provisos: that administration is delayed until the cervix is dilated at least three fingerbreadths; that if the labour is not completed at the end of six hours the administration is stopped; and diminution in strength and frequency of the uterine contractions is an indication for discontinuing the administration.

I wish to thank the midwives for their co-operation and assistance in completing the forms.

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The St. John Ambulance Association has published a booklet designed to show older children the importance of personal hygiene and the hygienic handling of food. It is intended as the basis for the association's preliminary course on these subjects. The booklet, which has been written by Dr. Guy Bousfield, may be obtained from the association at St. John's Gate, London, E.C.1, price 1s. 6d. (by post 1s. 8d.).

Medical Memoranda

A Case of Primary Red-cell Aplasia

Primary aplastic anaemia is a rare condition occurring usually before the fourth decade. All the elements of the bone marrow are depressed, and the consequent symptoms of anaemia, with mouth infection and haemorrhage into skin and mucous membrane, have been long recognized. In recent years, however, it has been demonstrated that aplasia of bone marrow can occur which involves only the red-cell element. In view of the rarity of this condition it is of interest to record the following case.

CASE REPORT

A male infant aged 11 weeks was referred to hospital on July 3, 1950, because of extreme pallor. It was stated that the pregnancy and delivery had been normal, and that he had weighed 7 lb. (3.2 kg.) at birth. The mother declared that the child had been slightly yellow on the first day of life and had remained so for two or three days. Pallor had been noticed some weeks before admission, but it had grown steadily worse. There were two other children. The first had died of pneumonia at 7 months, and the mother stated that it also had been slightly yellow on the first and second days of life. The second baby was healthy and of normal colour. The mother and father were in normal health.

The baby, which weighed 10 lb. (4.5 kg.), was seen to be very pale. There was no icterus; neither liver nor spleen was palpable, and there were no other abnormal physical signs. A green stool was passed soon after admission, but subsequent stools were normal. Blood examination on July 3 showed: haemoglobin, 16%; red cells, 630,000; white cells, 5,850, with 41% polymorphs. The red blood cells showed macrocytosis, anisocytosis, and poikilocytosis. The blood was Group O, rhesus-positive. The mother's blood was Group B, rhesus-positive. Tibial marrow examination showed "moderate cellularity, red-cell precursors almost entirely absent, an occasional normoblast (less than 0.5%), and no gross abnormality of white cells. Apparently a pure red-cell aplasia." The blood W.R. and Kahn test were negative, and *x*-ray examination of the long bones revealed no abnormality.

Blood transfusions were given at intervals of three to five weeks. He was also given iron and folic acid by mouth, and liver by intramuscular injection, which proved ineffective. The baby has continued to develop well, and usually seems happy until the haemoglobin drops below 40%. At the time of writing he is 18 months old and in good health, having had no illness except mild diarrhoea once in the past three months. Further bone-marrow examinations confirmed the diagnosis.

COMMENT

Clinically this case was one of severe anaemia. There was no history of blood loss, and examination of the bone marrow showed that the essential defect was failure to produce red cells, and red cells only.

Prior to 1932 three cases of pure red-cell anaemia had been described (Kaznelson, 1922; Baar, 1928; Lupu and Nicolau, 1931). Since then, however, further cases have been put on record. Diamond and Blackfan (1938) described four cases, with recovery in one case after two years' treatment with blood transfusions. Numerous substances were given by mouth in the hope of stimulating erythropoiesis, but none were successful. Splenectomy, performed at 16 months, produced a remission in one case. They thought that aetiological factors involved were probably either congenital deficiency of red-cell element of the marrow or a defect in the metabolism of the blood.

Macfarlane and Currie (1943) described a case occurring in a woman aged 22 who died of fatal pyrexia following a blood transfusion. Rinvik (1941–2) described two cases in infants between 2 and 3 months who were kept alive for long periods by blood transfusions. Robson and Sweeney (1948) described a case of red-cell aplasia arising in a child of 18 months.

Smith (1949) refers to the condition as chronic congenital aregenerative anaemia. He postulates prolonged depression of the red-cell elements of the marrow by an antibody formed during foetal life. This antibody is thought to be due to ABO incompatibility between mother and child—for example, the infant's group being A and the mother's O. The history of jaundice shortly after birth would make this theory attractive in our case, but the patient's being Group O militated against the hypothesis. Further test showed no incompatibility between the child's cells and the mother's serum.

I am indebted to Dr. R. D. C. Johnstone for permission to publish this case, and to Dr. F. Graham Lescher for his advice and encouragement.

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Immediate Death after Intravenous Injection of Iodoxyl

Death following the intravenous injection of contrast media for pyelography is very rare. When it does occur it may be immediate or delayed, the immediate death being due to reaction to the drug, and the delayed death being due to pre-existing severe renal damage, which may or may not be aggravated by the injected substance. All immediate deaths hitherto reported in the literature have followed the injection of diodone (3:5-di-iodo-4-pyridone-N-acetic acid and diethanolamine), and none so far have been reported after the administration of iodoxyl (disodium-N-methyl-3:5-di-iodo-4-pyridoxyl-2:6-dicarboxylate). The following case, therefore, is of interest in that a fatal anaphylactic type of reaction occurred after the injection of this drug.

CASE REPORT

A technical mechanical engineer aged 53 was admitted to hospital on September 8, 1951, for investigation of diarrhoea, vomiting, and swelling of the left leg. These symptoms had been present for three weeks. There was nothing relevant in the past history: his general health had been good and his weight was steady.

Physical examination revealed a large fixed mass in the pelvis and gross oedema of the left leg, extending to the groin. There were no other abnormal physical signs. His blood pressure was 150/90, and Hb 92% Haldane (13.6 g.%). Urine: reaction acid, no albumin or sugar, culture sterile. Blood urea, 15 mg. per 100 ml.; serum protein, 6.48 g.%.

Sigmoidoscopy under anaesthesia revealed no growth. It seemed probable that the oedema was due to pressure of the mass on the vessels of the left leg, so intravenous pyelography was ordered to exclude ureteric obstruction by the mass.

On September 13 20 ml. of iodoxyl solution ("pyelectan") was injected intravenously. The solution had been warmed to 37° C. and was given slowly (three to four minutes). During the injection the patient was asked whether he felt any ill effects, particularly pain in the arm, which often occurs with this preparation. The complete absence of any local reaction was remarked upon at the time. As the radiographer was about to take the five-minute picture she noticed that he failed to co-operate. He complained of dyspnoea, a tight feeling in the chest, and a desire to defaecate.

On examination he was dyspnoeic and his pulse was weak, fast, and irregular. Nikethamide, 3.5 ml., was given intravenously at once, with slight improvement, and he was returned to the ward immediately. By the time he arrived in bed (10 minutes after the injection) he had become intensely dyspnoeic and moist sounds could be heard all over the lung fields. He began to expectorate a large amount of frothy sputum. His pulse was now imperceptible and there was marked peripheral circulatory failure, with deep cyanosis. Atropine, 1/33 gr. (2 mg.), and morphine, 1/16 gr. (4 mg.), were given intramuscularly.

In spite of all efforts at resuscitation (oxygen, artificial respiration, and aspiration of the pharynx) his condition deteriorated rapidly and he died three-quarters of an hour from the time of the injection.

Post-mortem Report.—A well-nourished man. No external injuries. Heart: muscle rather flabby and fatty, otherwise normal. Lungs: acute oedema present; all air passages full of pale frothy fluid. Liver: slightly congested and slightly fatty. The spleen and kidneys were congested. The bladder was normal. In the pelvis was a small collection—a few drachms—of thick yellow pus arising from a perforated diverticulum of the rectum. There was an area of induration around the bowel, but the mucosa was normal. The stomach and intestines were otherwise normal. Oedema of the left leg was present, but no thrombosis was found. *Cause of death:* acute pulmonary oedema and myocardial degeneration accelerated by perforation of diverticulum of the rectum.

COMMENT

The empty ampoule and the remaining full ampoule of the box were returned to the manufacturers for analysis, and were found to be pharmacologically pure.

Pendergrass *et al.* (1942), in their survey of 661,800 pyelographic examinations, record 10 immediate deaths—all following the administration of diodone. Of these, three presented a clinical picture and necropsy findings very similar to the above case.

The cause of the reaction is obscure, but it is now generally agreed that it is not due to the iodine in the compound, but to some other part of the molecule. Thus, Gautot (1950) suggests that these are anaphylactic reactions, and that the sensitizing agent is diethanolamine in the case of diodone. He points out that this substance is used in the manufacture of many toilet and household preparations, and that from these sensitivity is acquired.

No reliable test for sensitivity has so far been discovered, and the prevention of an occasional very severe or even fatal reaction in a healthy patient with normal renal function seems to be impossible at present.

If the condition is recognized at once adrenaline should be given. However, in the present case it was not until the patient had developed acute pulmonary oedema that the true nature of the condition was recognized; at first, either a coronary occlusion or a pulmonary embolus appeared more likely. Even if treatment is given promptly, as it was in most of the cases so far reported, it seems to have little or no effect upon the course of the illness in the fatal case.

I wish to thank Mr. Kenneth James for permission to report this case, and Messrs. Glaxo Laboratories Ltd. for their help.

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Reviews

PROGRESS IN ENDOCRINOLOGY

Ciba Foundation Colloquia on Endocrinology. Volume 1: Steroid Hormones and Tumour Growth and Steroid Hormones and Enzymes. Volume 2: Steroid Metabolism and Estimation. Volume 3: Hormones, Psychology and Behaviour and Steroid Hormone Administration. Volume 4: Anterior Pituitary Secretion and Hormonal Influences in Water Metabolism. General Editor for the Ciba Foundation, G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., assisted by Margaret P. Cameron, M.A., A.B.L.S. (Pp. 1,716. 30s., 35s., 35s., and 45s. respectively.) London: J. and A. Churchill. 1952.

In recent years increasing use has been made of the colloquium to enable research workers in a particular field to discuss together their progress and their problems. The main purpose of such colloquia is the airing of difficulties, and papers submitted therefore tend to serve a rather different purpose from those published in the scientific and medical periodicals. In the colloquium, for example, the subsequent discussion of a paper may sometimes be more valuable than the paper itself. To be effective such conferences must be restricted to a relatively small number of experts and must be rather informal. Inevitably many workers in the subject will be excluded from attendance.

The Ciba Foundation in London is to be congratulated on the very successful manner in which it has organized and sponsored a series of such colloquia on various subjects and has been able to ensure a genuinely international representation. Many of these have been on matters related to steroid and pituitary hormones, and the reports of eight conferences on steroids are now published in the four volumes under review, so that the full discussions may be available to a wider audience.

The number of papers, each with its subsequent discussion, is so large that no adequate mention can be made here. The first conference is on hormones and tumour growth. Most of the papers relate to animal experiments, but two are devoted to the use of oestrogens in human cancer control, and a third to the use of cortisone and A.C.T.H. in acute leukaemia in children. In the second conference, on steroids and enzymes, many papers are concerned with the functions of β-glucuronidase in synthesis of glucuronides, but several other enzymes are discussed. In the conference on estimation of steroid hormones five papers are devoted to pregnanediol excretion and estimation, eight to the chemical methods of estimation of oestrogens, and one to the metabolism of radioactive oestrogens. Many papers also are devoted to the difficulties of extraction and estimation of urinary so-called adrenal steroids. A major conclusion in this section is that no satisfactory technique is yet available for extracting such adrenal steroids from urine and that indeed "no worker at the present time is estimating the total urinary corticoid." The reasons for such a conclusion are well discussed. The fourth conference deals mainly with the intermediate metabolism of the steroid hormones. In the conference on hormones, psychology, and behaviour the influence of hormones on sexual behaviour and drive are fully considered. Apparently sexual performance in the male is far more dependent on an intact cerebral cortex than it is in the female. An interesting study shows that the wild rat, exposed to the frequent stresses of its natural life, has far larger adrenal glands than its sheltered cousin the laboratory rat. Interesting speculations are made on the possible comparable effects of civilization on the adrenals of man. The authors of some papers discuss at length the effects of hormone therapy and of endocrine disease on personality, others study endocrine function in patients with established mental disorder. Qualitative and quantitative differences are found in schizophrenia. The sixth colloquium is on modes of hormone administration. The graphic method of displaying oestrogen action on the feathers of fowls is well illustrated in a series of plates, and several studies are reported of the rate of absorption of steroid from implanted pellets in man. Useful clinical data are presented in this section.

The conference on anterior pituitary secretion comprises 37 papers and their discussions. It deals with the cells in the pituitary originating the various hormones, the hypothalamic paths of pituitary control, the bio-assay of the various hormones, the fate of tracer-labelled pituitary hormones, and many allied aspects. The eighth conference, on water metabolism, presents 15 papers covering excretion of sodium, water, acids and bases, and so on. It includes evidence suggesting the presence of a sodium-retaining hormone in human urine.

The very large amount of information in these volumes is of interest primarily to research workers and others interested in the technical problems concerned. Much of it is difficult to obtain elsewhere. The books are well produced, but it is disturbing to find that about two years have elapsed between the holding of many of these colloquia and their appearance in book form. In a research field as active as endocrinology this is far too long an interval, and speedier methods of publication must be found if these reports are adequately to serve the purpose for which they are intended.

C. L. COPE.

MEDICAL MYCOLOGY

Medical Mycology: An Introduction to its Problems. By G. C. Ainsworth, B.Sc., Ph.D., F.L.S. (Pp. 105; illustrated. 15s.) London: Sir Isaac Pitman and Sons. 1953.

In about 100 pages the author makes a commendable effort to introduce to students of mycology, medicine, and microbiology the history, pathogenesis, epidemiology, and clinical aspects of fungous diseases. The book is a useful introduction to classical and recent literature, but the absence of reservation when referring to certain published works may give rise to misleading impressions. Minor inaccuracies, too, arise from excessive summarization. *Cryptococcus neoformans*, for example, is described as producing no local tissue reaction, while, in fact, various degrees of subacute inflammation do occur in torulosis. Established clinical names like "tinea capitis" are criticized for being imprecise. But general terms for ringworm infections of this kind are found useful in practice, and the degrees of acuteness of inflammation produced by their various causative fungi are well recognized. Undue prominence is given to the virulence of *Candida albicans* by attributing to its invasion the death of infected children. Reference to this organism as a secondary invader in tuberculosis is unqualified. Therapeutic measures against moniliasis and aspergillosis are mentioned as if their efficacy was proved. It is more than can be expected from a work of this size, which deals with so much, that the incidence of mycotic infections in any one country could be made apparent. The author states that neither the mycologist nor the clinician alone is usually in a position to come to a correct decision on the right interpretation of fungi found in the sputum or associated with pulmonary disorders. This problem does not occur in practice. Sections are devoted to botanical taxonomy (on which Dr. Ainsworth is an accepted authority) and to serology. There is a useful chapter on allergy, and a place is found for the poisonous fungi. The structure of pathogenic fungi and the histological reactions they incite are not described.

R. W. RIDDELL.

USING THE LIBRARY

How to Use a Medical Library. By Leslie T. Morton, A.L.A. Second edition. (Pp. 44. 5s.) London: William Heinemann Medical Books. 1952.

To the student, using the library often enough means asking at the desk for a familiar book or periodical; if it happens to be "out," he grumbles and waits or chooses the next best thing. The doctor, especially if he is a research worker, is more resourceful. He has a vague idea that libraries do more than issue books, but it may take him years to learn,

in casual fashion, of the full range of services available to those who know how to ask for them. By buying this excellent little book he can anticipate experience and do himself—and librarians—a good turn. The author, formerly librarian of St. Thomas's Hospital Medical School and now information officer of the *British Medical Journal*, here provides a complete guide to all who use medical libraries—students, doctors, and research workers.

He begins by noting that work in the library is just as important as bench work—a point not always fully appreciated. Later chapters are on the geography of a library, sources of information and how to use them, the location of works not possessed by the library, references, catalogues, periodicals, and abstracts. The last chapter, based on Le Fanu's directory, is an up-to-date guide to the chief British medical libraries.

The information is comprehensive and the advice in the main sound. The style is close-knit, and most of us will have to read the book more than once to understand it—not an easy task because of the very small type. When looking up the literature on any topic, surely it is best to get the latest review and to work back. This, so far as I know, is standard practice, but it gets three lines, as against the page or so for the appalling method of starting at the year dot and working forward. The research worker can no more delegate his bibliographic work than a surgeon can his operating—if he has any self-respect. In fairness to authors, original papers should always be studied, because abstracts are of necessity selective and do not provide a satisfactory basis for criticism of their work. The book will serve its main purpose admirably; may it also bring home to many the grievous blow medicine has suffered by the stoppage of the *Index-Catalogue*.

RAYMOND WHITEHEAD.

PSYCHIATRY AND THE STUDENT

Psychiatry and Medical Education. Report of the 1951 Conference on Psychiatric Education held at Cornell University, Ithaca, New York, June 21–27, 1951. Organized and conducted by the American Psychiatric Association and the Association of American Medical Colleges. (Pp. 164. No price.) Washington: American Psychiatric Association. 1952.

As a counter to increasing specialization in medical and scientific work it is now very fashionable to hold conferences for the exchange of views between the different branches. Advanced by the need for urgent solutions to technical problems in time of war, the method had considerable success, inspiring as it did a generous pooling of knowledge and the suppression of prejudice. It was soon recognized that it was in the preparatory commissions that the real work was done, and that the formal sessions tended to vagueness and platitude. Psychiatric education has a good precedent in this field, and the reports of the four annual conferences of 1933–6 on this subject give a very great deal of information, even if every school has since continued to develop in its own way. This book contains a well-edited report of the conference conducted in 1951 by the American Psychiatric Association and the Association of American Medical Colleges.

The subjects under discussion included the extent to which a student should, on qualification, be able to deal with personal problems as well as those of disease, the selection and preliminary training of students from the point of view of their later contact with the social and psychological aspects of disease, and the deficiencies in the present medical curriculum. The view appears now to have been accepted that teaching on mental disorders is of secondary importance to educating the student in the psychological aspects of physical disease and of his relation with his patients. In selection, the early enthusiasm for the use of tests and selection procedures instead of traditional methods has settled down to a useful compromise in which the value of character as well as mere intellect is recognized. Some remarkable figures are given for the incidence of personality problems requiring psychiatric help among medical students, amounting to nearly half in some studies, and it is refreshing to hear that at one school at least the students were "as a group rather hostile to psychiatric help."

The report is a readable but rather inconclusive presentation of the present situation in the United States, and it contains much experience from which we in Britain could benefit. It would be a pity if medical-school authorities expressed any strong views without first reading this book and being aware of the excellent bibliography on the subject. A selection of original papers likely to be of use to those concerned in designing the medical curriculum is given at the end of the book, and sets of these have been reprinted as a companion to the report.

ALEXANDER KENNEDY.

THERAPEUTIC THORNS

Side Effects of Drugs. By L. Meyler. Translated by Ph. Vuijsje and W. Mulhall Corbet. (Pp. 268. £1 10s.) London: Elsevier Publishing Co. 1952.

There are no potent therapeutic roses without their thorns. In this work the author has attempted to enumerate all the side-effects of various drugs in common use in the hope that the book will be useful in determining whether new symptoms arising in the course of certain diseases are due to the malady suffered or to the remedy given. The ambition is laudable, and one can imagine a work of reference of this kind being of the greatest service. The present volume, however, is the most extraordinary hotch-potch of information on the subject derived partly from original articles and partly from a study of the abstracts in *Excerpta Medica*. The facts are thrown together without any plan or arrangement in an utterly higgledy-piggledy and inconsequent manner interspersed with the most erratic punctuation. The translators have a somewhat sketchy knowledge of English, derived, it would seem, from an extensive study of Mr. Jingle's pronouncements. Little or no attempt is made to indicate the relative frequency of this or that side-effect or toxic reaction, their mode of production, or their prevention and treatment. A sentence describing some of the side-effects of "antabuse" will indicate better than any description the singular style of the book:

"The patients feel very sick, they have a throbbing headache; itching erythema; glycosuria. Fatal cases have been reported. A patient died after taking 30 ml. of rum; a marked dilatation of the right heart was found. Tetany due to hyperventilation; acute nephrosis. Persons taking antabus cannot use tonics and cough medicines in alcoholic vehicles; neither can they have massage with alcohol."

While the book has a certain charm because of its ingenuous quality and the amount of odd and alarming information which it contains, it can hardly be recommended.

D. M. DUNLOP.

Among new editions of British books that have appeared recently is MacKenna's *Diseases of the Skin* (Baillière, Tindall and Cox, 42s.). The fifth edition has been prepared by Dr. R. M. B. MacKenna, son of the original author, Dr. R. W. MacKenna. It is a textbook designed to meet the needs of student and practitioner, and has been completely revised. Many illustrations are included, some in colour. Dr. C. Langton Hewer has revised his *Recent Advances in Anaesthesia and Analgesia* (J. and A. Churchill, 30s.) for the seventh edition, and added a new chapter on the induction of hypotension to minimize blood loss during operations. Many chapters have been largely rewritten. In the thirteenth edition of Dr. W. M. Frazer's *Textbook of Public Health* (E. and S. Livingstone, 42s.) the author has made many changes in order to describe the effects of the National Health Service on the public health and hospital services. New material is also included on the National Assistance Act of 1948, and on the supervision of milk supplies. In the sixth edition of his well-known textbook *Medicine: Essentials for Practitioners and Students* (J. and A. Churchill, 37s. 6d.) Dr. G. E. Beaumont writes that he has endeavoured to omit what one of his reviewers referred to as the "organic nonsense" and the "historical nonsense" of medicine, and he has added much material on recent advances. There are new articles on, among other subjects, Q fever, temporal arteritis, anticoagulant drugs, headache, and the adrenocortical hormones.

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THE VESALIAN HERITAGE

Who are they whose work forms the foundation of scientific medicine? In judging special eminence opinions may differ, but few would dispute the claims of four men—Andreas Vesalius of Brussels (1514–64), William Harvey of Folkestone (1578–1657), Herman Boerhaave of Leyden (1668–1738), and Louis Pasteur of Dole (1822–95). On Vesalius, first of these great men in point of time, two works have appeared quite recently. One is *Three Vesalian Essays*, issued by the New York Academy of Medicine; the other, by Professor Singer, is *Vesalius on the Human Brain*, and is reviewed at p. 449.

Vesalius is a critical figure not only in the history of medicine but also in the history of thought and therefore in world history. His great book, *De Humani Corporis Fabrica* (1543), "On the Working of the Human Body," is a turning-point of the human spirit, for it set men on the task of exploring with their hands and eyes the intimate nature of living things. In it is clearly felt for the first time since antiquity the authentic and refreshing breeze of scientific research, conscious of itself and of its aims. In that book the systematic observation of Nature is set forth as a guide to the systematic control of Nature: *savoir afin de prévoir*. Foreseeing, *prognosis*, the Father of Medicine advised us more than two thousand years ago, lends peculiar confidence to the physician and peculiar power to his words. Anatomy, the only sure foundation of prognosis and the basis of all that is exact in medicine, must always look back to Vesalius. It is likely that Vesalian research and the flow of Vesalian literature will long continue, for the book of Vesalius is both enormous and difficult; it is a thing of such beauty that it must arrest attention in any library or museum; its author's life was linked with certain great movements of history; he was a spiritual wanderer between two worlds, the mediaeval and the modern. There are still many unsolved problems concerning both the man and his book, and their solution demands many kinds of knowledge seldom assembled in the same head.

For many years it had been known to a small circle that there survived some of the wood blocks of the figures in the great work of Vesalius. In 1932 the matter came to the ears of the late Dr. Samuel W. Lambert, a distinguished New York physician. On Lambert's action these blocks were ultimately discovered by Dr. Wiegand, of Munich, in the university library there. In 1934 they were used by the New York Academy of Medicine in conjunction with Munich University for their magnificent volume *Vesalii Icones Anatomicae*. This superb volume, itself a showpiece, contains all the figures associated with Vesalius and puts them within the reach of all who have access to a good library. This was none too soon. The service which the initiators of this noble tome were rendering to learning was greater than they knew, for the original blocks were utterly destroyed during the war.

A hardly less important production was Harvey Cushing's posthumous *Bio-Bibliography of Vesalius* (New York, 1943), which appeared at about the time that the blocks of Vesalius were themselves destroyed. Finally revised and certainly greatly improved by Professor John F. Fulton and his coadjutors, after Cushing's death in 1939, this work represents a constant interest of Cushing's, extended over more than 40 years. Every bibliographical detail that could be desired is included. It is an indispensable work not only for the life of Vesalius but for the study of a most eventful and critical period of cultural and political history.

Since the end of the war the rate of appearance of Vesalian literature has accelerated rather than slowed. Professors J. B. de C. M. Saunders, the anatomist, and C. D. O'Malley, the historian and Latinist, have long been collaborating in Vesalian research. In 1946 they produced an impressively documented translation of the difficult *Blood-letting letter of 1539*. Though this work of Vesalius is of little scientific significance in itself, it is perhaps the most important of all his writings for the understanding of the background of his life, his labours, and his personality.

In the same year the Wellcome Historical Medical Museum issued Professor Singer and Dr. Rabin's *Prelude to Modern Science*, a translation with running commentary of the *Tabulae Sex* of 1538, the first anatomical work of Vesalius. It displays the mental equipment with which he started on his great task and reveals much of the origin of our own anatomical nomenclature. We still lacked an English version of any considerable part of the *Fabrica*; Vesalius issued with it in the same year his so-called

Epitome of that work. This was intended not for medical but for "general" readers and perhaps especially for art students. It was rendered into English for the Historical Medical Library of Yale by Professor Lind in 1949, and is perhaps of most value for the light it throws on the adaptation by Vesalius of ancient Greek anatomical terms. It was followed in 1950 by the convenient quarto volume by Saunders and O'Malley, *The Illustrations from the Works of Vesalius*. This last contains the best account of the life of Vesalius together with translations of the captions of all the figures that he used and much other very valuable material.

The *Three Vesalian Essays* is now issued to accompany the *Icones* of 1934. In the foreword Dr. Malloch justly remarks that to many the impressions of the woodcuts in the *Icones* are even more beautiful than those in the original works from which they were prepared. The *Three Essays* open with a learned account by Dr. Lambert of the initial letters used by Vesalius. These are skilfully and often humorously decorated with human figures. They tell much of anatomical and surgical practice of the time. "Marginal Notes" by Dr. Willy Wiegand recount the story of the discovery of the lost blocks. Lastly Mr. Ivins eloquently expounds yet again his unconvincing and quite untenable theory that Vesalius was a nonentity whose sole originality was in choice of artist and that his text is of little value. In fact the Latin of Vesalius is difficult and verbose. This may explain why no substantial part of the *Fabrica* has been made available in English. However, in his *Vesalius on the Human Brain* Professor Singer has now provided a version in plain English of all on that subject that the *Fabrica* has to say. He has equipped it with an illustrated record of the debt that the account of the brain by Vesalius owed to its predecessors.

In looking at all these beautifully illustrated books the reader has constantly to remind himself that Vesalius had no means of preserving or hardening structures, and that he had hardly any effective predecessors since Galen, though it is true that he acknowledges inadequately such debt as he does owe them. Professors O'Malley and Saunders have long been at work on their translation of the complete text of the *Fabrica*. Its completion and publication must still take years—perhaps many years. When in due course it appears it will crown the series of *opera magnifica* which meanwhile not unworthily commemorate the great father of anatomy whose work is the foundation of all scientific medicine.

TRICHLORETHYLENE ANALGESIA IN LABOUR

Provision for pain relief during childbirth varies widely from country to country. At one end of the scale is Britain, with some form of analgesia available to every mother: at the other are countries where even leaders in the field of obstetrics hold the opinion—perhaps not always shared by their patients—that the pain of childbirth has a beneficial effect on mother and child and that relief is undesirable. It is sometimes held against us in Britain that so many home confinements are supervised by midwives, but a point in favour of our practice is that midwives are permitted, if not encouraged, to administer gas-and-air analgesia. This method, if it has not brought complete relief to more than a relatively small proportion of patients, at least has done few of them and their babies any harm. Moreover, ever since gas-and-air analgesia began to come into fairly general use by midwives in this country in the years immediately before the war there has been a restless search, perhaps stimulated by an insistent demand from the public, for an alternative method which could be equally easily and safely self-administered and which would be more effective in a greater proportion of cases.

Many are now pinning their hopes on trichlorethylene ("trilene"), the analgesic powers of which have been known ever since the first world war, when German workmen learnt the effects of inhaling the vapour as they leaned over degreasing vats containing the liquid. In recent years trichlorethylene has been used on an increasing scale both as an anaesthetic and as an analgesic, and its actions and effects are reasonably well understood pharmacologically and clinically. If numbers of administrations mean anything, it has proved itself a very safe anaesthetic and analgesic. A characteristic example of the careful and thorough investigations into the efficacy of trichlorethylene as an analgesic in labour is that of Seward,[1] who four years ago determined the effective concentrations of trichlorethylene in air, and concluded that it was a more satisfactory and powerful analgesic than gas and air, though he pointed out that its prolonged use might lead to some cumulation. The advisability of allowing midwives to use trichlorethylene has been under consideration for the last few years by a committee consisting of obstetricians, anaesthetists, midwives, and research workers. Difficulty has apparently arisen over which apparatus midwives should be allowed to use. Understandably, the desire

[1] *Lancet*, 1949, **2**, 781.

of the committee has been to make sure that any device approved for this purpose should deliver suitable, safe, and unvarying concentrations of the vapour. So far the committee has not yet given its approval to any apparatus. Commercial interests, however, alive to the possibilities of development in this field, have put several inhalers on the market. These are not only said to administer the concentration of trichlorethylene in air which clinical observation has determined to be effective, but also have a device which automatically neutralizes the effects of changes of temperature within the inhaler. On another page in this issue Dr. E. E. Rawlings describes his experiences with one such inhaler. He comes to the conclusion that the analgesia produced by it is satisfactory, but he adds a similar caution to that of Seward in advising against prolonged administration. For this reason he delays the administration of trichlorethylene until the cervix is dilated to three finger-breadths. On the basis of these two careful investigations alone—and there are others—it seems that perhaps there is still some justification for caution before allowing midwives to administer trichlorethylene on their own, not so much on the grounds that the inhaler is not mechanically all that it should be, but rather that trichlorethylene itself, by virtue of its cumulative effects, demands skill and judgment in the administrator which not all midwives would necessarily possess. It would in any case hamper the acceptability of an analgesic if the time for beginning its administration had to be fixed by any criterion other than the patient's sensations. Pain, being subjective, can hardly be related to some objective fact such as the dilatation of the cervix. Any acceptable method of analgesia should be usable as soon as the patient desires relief from pain, the intensity and nature of which only she can judge. In the meantime there is no reason why doctors should not continue to administer trichlorethylene analgesia in labour with one of the inhalers available. The accumulation of their experience will help to clarify still further the value and place of trichlorethylene in labour.

At least one expression of opinion on this vexed question will find general agreement—that in spite of the progress that has been made the alleviation of pain in labour remains an urgent and important task for all working in this field.

LEUKAEMIA IN DOCTORS

In the U.S.A. leukaemia has been found to occur much more frequently as a cause of death among radiologists than among physicians in general, and the excess has been associated with exposure to *x* rays.[1] The radiologists constitute less than 1½% of the medical profession, and it would be interesting to know whether physicians who are exposed only occasionally to *x* rays show any increased incidence of leukaemia in comparison with other professions. In Britain evidence on this point is lacking, and the Registrar-General's report on occupational mortality during the three years round the census of 1931 gave no conclusive indication of any such excess.[2] In the years 1930–2 there were five deaths among 25,063 physicians and surgeons between the ages of 20 and 65 compared with an expectation of three if the rates at each age had been the same as for all males; and there were three deaths at ages over 65 in a population of 4,838. In another professional group of similar size, clergymen and other ministers of religion, nine deaths occurred at ages 20–65 in a population of 25,721 compared with an expectation of three; and there were six at ages over 65 among 10,976. These figures were not suggestive of special risk from *x* rays at that time, and no more recent national figures are available; the occupational mortality analysis round the census of 1951 must be awaited.

In a recent paper Peller and Pick[3] have produced statistics derived from the obituary notices of physicians which appeared in the *Journal of the American Medical Association* during 1947–51, and have compared them with the official statistics of deaths in the United States in 1948. The cause of death was disclosed for a total of 11,481 physicians out of 14,516 whose deaths were reported, and 133 of the total were attributed to leukaemia and 1,426 to other forms of malignant neoplasm. The proportion of leukaemia to all causes of death among the doctors was 5% at ages under 35, 2.3% at 35–44, 1.1% at 45–54, 1.2% at 55–64, and 0.9% at ages 65 and over, compared with about 1.2, 0.8, 0.7, 0.6, and 0.4% respectively among all males according to official statistics. Proportionate mortality may be deceptive unless the death rates from all causes of the groups compared can be safely assumed not to differ appreciably. But the authors estimate that, after correcting for peculiarities in the age distribution, there was no appreciable disparity between the general death rates of physicians and the average for all males.

The Registrar-General's statistics of 1930–2 showed that in England and Wales mortality of physicians and surgeons from all causes was 8% below average at ages 25–34, 6% below at 35–44, 8% above at 45–54, and 11% above at 55–64. It is highly probable that this gradient of relative general mortality is now more pronounced than it was, and this might go some way to account for the diminution with advancing age in the proportionate mortality for leukaemia in physicians, from four times the average at 25–34 to about twice the average at 45–64. Neither this, nor the changes in the method of selecting the underlying cause of death which were made in the United States after 1949, seem to account for the excessive leukaemia death rate indicated in this study among doctors in the U.S.A. It is estimated, further, that among the physicians who were neither radiologists nor dermatologists the leukaemia

[1] Dublin, L. I., and Spiegelman, M., *J. Amer. med. Ass.*, 1948, **137**, 1519.
[2] Registrar-General's *Decennial Supplement for 1931, Occupational Mortality*, 1938, Table 4A. H.M.S.O.
[3] Peller, S., and Pick, P., *Amer. J. med. Sci.*, 1952, **224**, 154.

rate at ages between 35 and 74 was twice the average for all males. There remains the possibility that diagnosis and certification of leukaemia is more complete in respect of doctors than the general population, and, since this can neither be proved nor disproved, no firm conclusion can be reached at present. It is reassuring that by the same process of calculation the authors show that proportionate mortality from all other forms of malignant neoplasm among the physicians was substantially below that of all males at each age group between 40 and 75.

WORLD FOOD NEEDS

Over large areas of the world the supply of food remains less than it was before the war. This is the conclusion to be drawn from the Second World Food Survey undertaken by the Food and Agriculture Organization of the United Nations.[1] The first survey was made in 1946, when the world food position was at its worst, supplies were at their smallest, distribution most uneven, and hunger and outright famine most widespread. Since then, over the world as a whole, food production has expanded, but the increase has barely kept pace with the increased population resulting from a higher birth rate and, owing to the control of mass diseases such as malaria, a decreased death rate. Clear signs of any far-reaching changes in the scale of food production, essential for the improvement of nutrition, are lacking. In what are known as the O.E.E.C. countries—that is, the countries of Western Europe (except Spain and Portugal) and Greece and Turkey—if the total agricultural output was reckoned at 100 before the war, it is now 111. In the underdeveloped areas elsewhere in the world progress since the war ended has been much slower, and political disturbances in the Far East have hindered recovery. In striking contrast to the slow and painful progress in most of the other parts of the world, the high post-war output of North America stands out. In the United States, if again the pre-war figure be taken as 100, it is now 131, and in Canada 130. A quantitative estimate for the world as a whole shows the average food supplies, measured in calories, to be 6% lower than in the pre-war period. In the Far East, where nearly one-half of the world's population is concentrated, the decline is of the order of 10%. The large gaps between the better and the worse-fed nations have been widened. In India the calories supplied by the available food are 24% below the estimated need; in the United States 18.5% above the estimated need, and in the United Kingdom 17% above. To assess nutritional quality is more difficult than a quantitative reckoning, but surveys in most of the heavily populated regions of the world have provided evidence that diets are not satisfactory nutritionally.

The F.A.O. has worked out for each region of the world the gross quantity of foodstuffs that it should be possible to produce by 1960. One overriding consideration is that in seven years' time there is likely to be an 11% increase in world population, which is increasing by slightly more than 1% per annum. In Latin America, the Near East, and Africa the increase is about 2%, and in the Far East probably more than the 1% shown in statistics admittedly faulty. The largest increases of population are still taking place in areas where food supply is most seriously inadequate. On the other hand, the problem may be eased by the improvement in human efficiency resulting from successful public health measures. The attainment of the targets for 1960 assumes a favourable economic and political situation, financial and technical assistance for underdeveloped countries, and an immense capital investment.

[1] Food and Agriculture Organization of the United Nations. *Second World Food Survey*, Rome, 1952. Obtainable from H.M.S.O., London. Price 2s. 6d.

FEELING THE COLD

The patient who complains of the cold may have a poor circulation through the skin or a poor metabolic heat production, as in myxoedema, muscular hypotonia, or flaccid paralysis, since the musculature is an important heat-producing tissue. Lack of subcutaneous fat, as in malnutrition or wasting disease, allows the heat produced to leak away faster, while the thicker layer of fat normally present in women enables them to stand the cold better than men. Their heat loss is 10% less under the same conditions. Their skins are colder in cold weather, but warmer in the hot by over 1° C. than those of men, because they sweat less. Clothing is an important barrier against the cold provided it is dry, absorbs sweat easily, and remains porous, so that air is trapped as stationary poorly conducting air cells. To these well-known facts must be added one sometimes overlooked: cold sensations are relative. If the left hand is placed in a bowl of water at 20° C., the right hand in one at 40° C., and then both are transferred to water at 30° C., the same water feels cold to one hand and hot to the other. This raises the question of how we appreciate cold, and it has to be admitted that there is no satisfactory explanation of all the facts.

Cold and warmth are separately appreciated.[1] Different points on the skin respond either to cold or to warmth, and peripheral sensory nerves when treated with cocaine or asphyxiated or cooled lose the power to transmit cold or hot sensations separately and under different conditions.[2] Cold-sensitive spots are at least 10 times more numerous than heat-sensitive ones, and it seems probable that they are fixed in location in spite of the fact that their distribution appears to change from test to test. They are not all equally sensitive to a given cold stimulus, and their individual sensitivities are constantly changing. This accounts for spatial differences found in different experiments. Certainly in the outer part of the cornea, in much of the conjunctiva, and in the glans penis—all sites which lack most of the senses of ordinary skin—cold is appreciated by histologically distinct sense organs, the end bulbs of Krause; these are small solid spheres of epithelial cells among

[1] Wadsworth, R. S., *Experimental Psychology*, London, 1938, p. 454.
[2] Bickford, R. J., *Clin. Sci.*, 1939, **4**, 159.
[3] Hensel, H., *Pflüg. Arch. ges. Physiol.*, 1950, **252**, 146, 197.
[4] —— and Zotterman, Y., *Acta physiol. scand.*, 1951, **22**, 96.
[5] Ibid., 1952, **28**, 345.
[6] *Brain*, 1952, **75**, 325.

which the sensory nerve fibrils branch. Elsewhere in the skin, biopsy of cold-spots has not shown any special structure.

The normal temperature of exposed skin is about 30–32° C., and usually the cold-spots give rise to sensations of cold only below 30° C. Paradoxically, however, they also give rise to sensations of cold when heated to 45° C., care being taken not to warm the heat-spots at the same time. They also may respond to mechanical and electrical stimulation. Hensel has been able to show with the help of his delicate thermocouple introduced into different levels of the skin[3] that warm-spots continue to signal the heat long after the warmed skin has attained constancy at the new hotter temperature, while cold-spots in the tongue continue to send cold sensations when the tongue is kept constantly cold.[4] In fact Dodt and Zotterman[5] have demonstrated that these temperature sense organs send impulses up their nerves with a frequency which corresponds to the constant temperature, whatever it is. Further, they find that, in the cat's tongue at least, the heat spots cease to signal at temperatures over 47° C., and it is the cold spots in their paradoxical phase which then yield the sensation of heat.

How do these end-organs act like thermometers? Possibly, as O'Connor and McCarthy[6] have recently suggested, changes in the physical state of fatty acids in the skin with changes in temperature may have something to do with the response, but it must be remembered also that the metabolic reactions of skin and nerve, like all chemical reactions, double their velocity for every 10° C. rise of temperature. The refractory period of the sense organ will change, and also the nature and concentration of substances in the surrounding tissue fluid. There may also be changes in blood flow and sweat rate to reckon with, for the skin is an organ and not a homogeneous tissue. Hitherto most research on temperature sensations has been carried out on normal persons. Perhaps repetition of the experiments on people with metabolic and neurovascular disorders, or with skin diseases such as psoriasis, would help to clarify what is at present a complex problem.

NURSES IN HOSPITAL

A model piece of research following upon the report, published in 1947, of the Working Party on the Recruitment and Training of Nurses has been undertaken by the Nuffield Provincial Hospitals Trust in the shape of a job-analysis of hospital nursing.[1] The work has been carried out by seven field investigators under the directorship of Mr. H. A. Goddard, with the help of an advisory panel of which Sir Ernest Rock Carling has been chairman. The investigators have directed their attention to the pattern of hospital ward work, the allocation of duties among different grades of nurses, and the manner in which the needs of patients are met. Twelve general teaching hospitals, covering a wide geographical area, were taken for the purpose, and about a week was spent in each of the medical and surgical wards selected for observation.

A distinction is made at the beginning of the latest report between basic nursing—by which is meant the care required for the well-being and comfort of the patient irrespective of the disease from which he is suffering—and technical nursing, a term which describes the special care given on account of the disease. Basic nursing was found to take up rather more than two-thirds of the nurse's time, and technical nursing just under one-third. The view of those responsible for this report is that the two functions cannot be separated and assigned to different individuals. Obviously the patient's physical comfort and freedom from mental worry may be as important a factor in his recovery as any technical treatment, and his nursing needs in both respects must be met by the same person.

It is sometimes said that the doctor claims an undue proportion of the time of the ward staff, but it was found on analysis that the time spent by the nurse with doctors averaged less than half an hour per bed per week. Consultants, in this observation at least, were always escorted by nursing staff, but in the case of house officers the practice varied. Allied with this was the vexed question of early wakening in the wards. The determining factor is the routine tasks to be completed before the doctors' rounds, which may begin at 9 a.m. In 18 of the 22 wards investigated patients were wakened before 5 a.m. A study of the rounds of visits showed that of 350 rounds by consultants 43 began before 10 a.m., a few before 9 a.m., and on 21 occasions house-physicians and house-surgeons visited the wards before the earlier hour. In two-thirds of the wards consultants' rounds were between noon and 2 p.m., the peak hours for basic nursing. Some ward sisters said that they had established the precedent that there should be no rounds during patients' mealtimes.

Student nursing figures largely in this investigation. Shortages of trained nursing staff or domestic workers react on the student nurse, who has to make good most of the nursing deficiency. So long as student nurses comprise more than half the labour force in the wards it is inevitable that their training should on occasion be subordinated to administrative necessity. The term "student nurse" is misleading; she is employed in the ward, but not specifically taught. The report states that maximum use is not made of the grade of ward orderly. Many people now filling the domestic post of ward orderly would be well qualified with suitable training to hold auxiliary nursing posts. Actually 25,000 ward orderlies are employed in the hospitals in this country, and there would be no difficulty in most areas in increasing the number, whereas assistant nurses are not coming forward in as large numbers as was hoped. To avoid the present excessive dependence on student nurses it is urged that more nursing auxiliaries be recruited from the labour sources which now provide ward orderlies, and, in the words of the advisory panel, the practical work entrusted to the student nurse should be planned in accordance with her training needs and carried out in conjunction with trained staff.

[1] *The Work of Nurses in Hospital Wards. Report of a Job-Analysis*, 1953. London.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

MISCARRIAGE

BY

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In this article the terms miscarriage and abortion are synonymous, and refer to the termination of pregnancy before the twenty-eighth week of intrauterine life. The incidence of spontaneous abortion in this country probably varies between 8 and 10% of all pregnancies. It is difficult to assess the frequency with which abortion is induced criminally, but the figure is high, particularly in the large cities, and it is this type of abortion which has the highest morbidity and mortality.

Causes

The commonest cause of spontaneous abortion is an abnormality of development of the foetus or trophoblast which is severe enough to cause death. This condition is in most cases a non-recurring factor, and the patient has an 80 to 90% chance of going to full term on the next occasion. For this reason it is safe to reassure the patient who has miscarried for the first time that her next pregnancy will most likely be uneventful. The mother is always anxious for a reason why she has miscarried, and it is safe to tell her that the most likely cause of a single miscarriage is a developmental abnormality of the foetus, so that it is as well that it did not survive. Reassurance is then given that such abnormalities are most unlikely to recur in subsequent pregnancies. Needless to say, this advice should not be given when the patient is still suffering only from a threatened miscarriage.

Probably the second commonest cause of miscarriage is an abnormality either of hormonal balance or of development of the uterus. In the former case the ratio between pituitary and placental hormones and oestrin and progesterone secretion is abnormal. In the latter case the uterus, being deficient in development, becomes more and more irritable as the cavity is stretched by the growing foetus, so that it begins to contract and retract, thus discharging its contents.

Diabetes, chronic nephritis, the acute specific fevers, and any disease which produces an acute toxaemia are less common causes of abortion. There is little evidence at present that rhesus incompatibility is a cause of miscarriage in the first three months of pregnancy. An acute emotional upset undoubtedly can cause the uterus to evacuate its contents.

A fibromyoma of the uterus may cause a miscarriage if it is submucous in distribution. However, many women with small uterine fibroids which are not submucous both succeed in becoming pregnant and in having a normal labour. Retroversion of the uterus is often associated with early pregnancy, but the malposition itself is rarely the cause of abortion. If abortion should be threatened or become inevitable in a first pregnancy, then the accompanying hypoplasia of the uterus is the more likely cause.

Thyroid deficiency may be a cause of miscarriage, but it is unjustifiable to administer thyroid unless clear evidence of deficiency is present. It is very doubtful if deficiency of vitamin E is ever a cause of infertility or miscarriage, at least in Britain.

Threatened Abortion

The symptoms of this condition are well known: bleeding from the uterine cavity, with or without a dull backache suggestive of the onset of menstruation, or even the presence of rhythmical uterine contractions. It is wise to pass a speculum with great gentleness to make sure that the haemorrhage is not caused by a mucous polypus or even a carcinoma of the cervix. It is important to cause the patient as little discomfort as possible; a well-lubricated Fergusson, or duckbill, speculum should be passed upwards and depressed backwards until the cervix is exposed. It is common to have difficulty in finding the cervix because the speculum is passed into the anterior fornix.

The type of bleeding in threatened abortion is of interest. The haemorrhage comes from either the potential cavity in the decidua lining the uterus, which is present until the ovum fills the whole cavity at the third month, or more often from the attachment of the foetal trophoblast to the decidua basalis or the decidua capsularis. In either case the haemorrhage is at first bright in colour. If this continues to be bright red and increases in amount the prognosis is correspondingly less good. A single bright loss followed by the escape of old brown blood merely means that an initial haemorrhage has occurred but none since. It is not uncommon in threatened abortion after the third month for such a dark brown blood loss to go on for one to two weeks. This can usually be taken to mean that the foetus is growing satisfactorily; as the foetus grows it squeezes out the remaining old blood from the uterine cavity.

The amount of blood loss and pain which can occur without the abortion becoming inevitable is surprising. All cases should be treated as threatened unless there is very good evidence for saying they are inevitable.

With a threatened miscarriage the patient should stay in bed for five days after the bright red haemorrhage has ceased. The loss of dark brown blood is not a reason for keeping her in bed. There are few households now where a patient can be given a bed-pan on these occasions, and it will do her little harm if she is encouraged to use a commode or to go to the lavatory when necessary. Otherwise she should stay strictly in bed. It is important to give the patient paraffin or any mild aperient which suits her so that she does not have to strain at stool. Administration of sedatives is important. An initial dose of morphine, ½ gr. (11 mg.), is advisable if the patient is much upset, and then phenobarbitone, 1 gr. (65 mg.) or less, three times a day, should be given for the next few days. Opinions differ so much on the vexed question of hormone deficiency in these cases that it is difficult to be dogmatic on this subject. The chances of a spontaneous recovery are high, and it is doubtful whether the administration of progesterone will be of any value, but the injection of 10 mg. on alternate days for five doses can do no harm. The use of anterior pituitary and chorionic gonadotrophic hormones is valueless.

When the patient has recovered she should be warned to take great care at the next two period times and to avoid coitus for the next three months.

Inevitable Abortion

A threatened abortion becomes inevitable when the bleeding increases greatly and uterine contractions become rhythmical and strong. The cervix then begins to dilate and products of conception may sometimes be felt protruding through the external os. Before the third month it is quite common for the foetus and trophoblast to be extruded intact when the abortion becomes complete. At about the third month the membranes often rupture and the foetus is passed, leaving the placenta behind, and all the complications of an inevitable incomplete abortion may arise.

It is of vital importance therefore to encourage complete evacuation of the uterus and to conserve blood loss

as much as possible. Everything that is passed per vaginam should be kept for examination; in this way it is often possible to establish that the abortion is complete. The passage of a decidual cast in a case of ectopic pregnancy may be mistaken for products of an intrauterine conception.

Treatment consists in complete rest in bed, which of itself lessens the amount of bleeding. An intramuscular injection of ergometrine, 0.5 mg., should be given four-hourly for three doses, and may be repeated in the next 12 hours. The use of oxytocin, 5 units (0.5 ml.), may be substituted for ergometrine, but the latter has a more prolonged effect on the uterine muscle. Posterior pituitary extract or vasopressin should never be used. Apart from maintaining asepsis as much as possible there is no other treatment to be given in a complete miscarriage other than the administration of the liquid extract of ergot, 1 dr. (3.5 ml.), thrice daily for a few days, as involution of the uterus is slow after abortion.

Inevitable Incomplete Abortion

This condition may create one of the worst emergencies that any practitioner has to deal with. It is possible for a woman to bleed so severely within the space of a few hours that the haemoglobin level drops to 20 or 30%, and often accompanying this is a severe degree of shock. If a patient is moved to hospital by ambulance before the shock is treated the latter may increase to a dangerous degree so that resuscitation becomes impossible. Such patients require immediate first aid, and if a flying squad is available this should be called upon to administer blood in the house before an ambulance takes the patient to hospital. The blood pressure should be taken and ergometrine, 0.5 mg., be given at once by intramuscular injection. The patient should be encouraged to take warm sweetened drinks and should be kept reasonably warm; the foot of the bed should be raised and morphine ¼ or ⅓ gr. (16 or 11 mg.), given. When the blood pressure has reached a more normal level the patient should be transferred to hospital.

In some cases an incomplete abortion is not associated with severe bleeding, but the haemorrhage continues intermittently for many weeks and is due to a placental polypus. The uterus remains bulky and the cervix slightly dilated. Surgical evacuation of the uterus is then essential, and the patient should be admitted to hospital.

Sometimes it is difficult to decide whether prolonged irregular bleeding after a miscarriage is due to a placental polypus or to a complete abortion followed by an anovular type of bleeding from the endometrium. This may occur before the ovarian cycle is re-established normally. In either event, if the haemorrhage does not cease after a reasonable time a curettage is the best and most efficient form of treatment.

Septic Abortion

The uterine cavity may become infected before an abortion begins. This is often the result of a criminal attempt to produce abortion by an instrument in the cervical canal. The patient presents with severe suprapubic pain and a raised temperature and pulse rate. There may be no bleeding or uterine contractions and the cervical canal remains closed. There is some rigidity of the abdominal wall spreading outwards and upwards from the pelvic brim. The uterus is exquisitely tender on bimanual examination. Unlike puerperal intrauterine infections the organism in cases of septic abortion is often the staphyloeoccus and not the haemolytic streptococcus. Other organisms may also be present, such as *Bact. coli* and *Streptococcus faecalis*. An anaerobic streptococcal infection is not uncommon and gas-forming organisms may also be found. Massive doses of crystalline penicillin, 500,000 units six-hourly, should be given, together with a sulphonamide, until the symptoms and signs subside. It is wise to continue the antibiotic treatment for at least five days after the temperature has reached normal. A sterile throat swab should be used to obtain a specimen of secretion either from the vault of the vagina or from the cervical canal through a vaginal speculum as soon as the patient is first seen. This is particularly necessary at present, because it is now common to find penicillin-resistant staphylococci. The swab should be sent to the laboratory at once for culture and to determine the sensitivity to antibiotics and sulphonamides. After the temperature has subsided the uterus may be left to evacuate itself spontaneously if the ovum is dead.

In cases of inevitable incomplete septic abortion the treatment may be of two kinds. First, the infection may be treated as described above and, if necessary, a blood transfusion given (with iron by mouth) to combat the anaemia. When the infection has been cured the uterus is then evacuated—by surgical means if oxytocic drugs fail. The theoretical advantage of this line of treatment is that the protecting mechanism, consisting of a zone of plasma cells and polymorphonuclear leucocytes in the uterine wall, is left intact while the infection is still present. The disadvantage is that haemorrhage may be severe, and dead placental tissue and blood clot in the uterus are excellent media for the growth of organisms, particularly of the anaerobic variety.

Secondly, it is possible to start giving the antibiotics and sulphonamides at the same time as ergometrine, and then after a short time evacuate the uterus surgically if necessary. It is common for the temperature and pulse rate to drop dramatically after the removal of a large piece of placenta which has been blocking the internal cervical os and allowing pus to collect above it.

Septic abortion, particularly in virulent infections, may be complicated by a spread of the organisms from the uterine cavity, causing salpingitis, peritonitis, parametritis, or septicaemia. In self-induced abortion the infection may reach the peritoneum directly owing to the passage of an instrument through the pouch of Douglas. If the instrument is passed into the cervical canal with the woman in the squatting position, perforation of the fundus may occur, but penetration sideways into the broad ligament is more likely to take place. This may produce an acute parametritis. A strange variety of instruments have been used in self-induced abortion, and any of these may be passed by mistake through the urethra into the bladder. In view of the dangers associated with septic abortion it is probably better to admit these cases to hospital for treatment. The medico-legal aspects of abortion have been discussed by Dr. Donald Teare in an earlier contribution to this series (see *Journal*, April 26, 1952, p. 915).

Missed Abortion

The formation of a carneous mole is uncommon. In these cases the patient usually notices a little bloodstained discharge for a day or two at about the eighth to the twelfth week of pregnancy. After this the breasts cease to be tender and swollen, but the patient often pays no attention to this. It is necessary in all cases of pregnancy to examine the abdomen at the fourth or fifth month in case the uterus has ceased to increase in size after the third month. A carneous mole can remain in the uterus for many months, and if it is not diagnosed the mother may have everything ready for the baby, only to be told late in pregnancy that the foetus died in the first few weeks. In cases of missed abortion the breasts show no signs of recent activity and the uterus ceases to grow from the date of the small haemorrhage. A pelvic examination reveals a firm uterus usually smaller than that of a three-months pregnancy. The uterus is filled with laminated blood clot with a shrunken amniotic sac in the centre. The biological pregnancy tests become negative about 10 days after the death of the ovum in these cases, and a pregnancy test should be carried out to confirm the diagnosis if this is made shortly after the vaginal haemorrhage.

All cases of carneous mole undergo spontaneous evacuation eventually, but sometimes it is many months before this happens. Massive doses of oestrogenic preparations never cause sensitivity of the uterus to oxytocic drugs when

the foetus is alive, and it is doubtful if they do so even when the foetus is dead. It is probably wiser to leave the uterus to evacuate itself spontaneously. If the patient is distressed by the knowledge that she is carrying about a dead foetus the uterus may be emptied surgically, using either laminaria tents or ovum forceps.

Vesicular Mole

This condition is one of the rarer causes of abortion, but it is of great importance because of the severe haemorrhage and sepsis which may occur and because a chorion epithelioma may develop. The patient usually begins to bleed between the eighth and the twelfth week of pregnancy. The uterus is always much larger than it should be, reaching nearly to the umbilicus, except when it is associated with a missed abortion. It is doughy in consistence and a little tender. If vesicles are seen in the blood lost from the vagina the diagnosis is established, but unfortunately these are not often found.

It is quite easy to make a mistaken diagnosis of vesicular mole. The differential diagnosis amounts to a mistake in the date of the last menstrual period, multiple pregnancy, pregnancy and fibroids, or pregnancy and an ovarian tumour. The diagnosis is established by having a quantitative biological pregnancy test performed. A morning specimen of urine should be collected and the pathologist requested to carry out the test in undiluted urine and in a dilution of 1 in 200. If the test is positive in both cases a vesicular mole is almost certain to be present. A normal pregnancy at about the third month sometimes gives a positive biological pregnancy test in a dilution of 1 in 100.

The evacuation of a vesicular mole requires great skill and judgment, and the patient should always be admitted to hospital for this. If the abortion is spontaneous it is almost the rule for some vesicles to be retained in the uterus, and it is wise to curette these patients as a routine procedure two weeks after the spontaneous evacuation. The patient is never safe until the pregnancy test is negative, and this test should be repeated at four-weekly intervals until it is so. If the test remains positive and perhaps in increasing dilutions the danger of chorion epithelioma is great. A further pregnancy should be discouraged for at least six months to avoid confusing the issue.

Habitual Abortion

By definition this refers to any case in which three consecutive spontaneous miscarriages have occurred. It can be shown statistically that a woman who miscarries for the first time has about an 87% chance of going to full term the next time she is pregnant. A woman who has had two consecutive miscarriages still has a 63% chance in the next pregnancy, but after three consecutive abortions the chances of reaching full term on the fourth occasion drop to 16%.

In habitual abortion the cause is usually of maternal origin. It has been suggested that it may be due to deficiency of progesterone secretion, and good results are claimed from the use of progesterone or, alternatively, of high doses of stilboestrol, which are believed to stimulate progesterone secretion. It is difficult to be dogmatic about these treatments, as there are many conflicting opinions on them. Vitamin E has also been tried in these cases, but there is no convincing evidence of its value. If the basal metabolic rate is below minus 10, thyroid deficiency may be the cause of abortion and thyroid should then be given.

In cases of habitual abortion a hysterogram should be done to exclude an abnormality of development such as a septate uterus, but any such condition is seldom found to be the cause. Fibromyomata of intramural or submucous distribution should always be removed if found in a case of habitual abortion. Deep cervical lacerations may cause miscarriage and should be repaired. Retroversion of the uterus should be corrected, if possible before pregnancy occurs, by the insertion of a Hodge pessary so that the pregnant uterus will not drop further back into the hollow of the sacrum. Only very occasionally is a ventrisuspension justifiable, as the retroversion is often associated with a generalized hypoplasia of the uterus, which is likely to be the real cause of habitual miscarriage.

A popular treatment at present consists in the implantation of progesterone pellets. Six pellets, each of 25 mg., are introduced below the deep fascia covering the gluteal muscles or under the fascia covering the lateral aspect of the thigh. A general anaesthetic is advisable. If the pellets are placed more superficially they will find their way to the surface. Alternatively, stilboestrol may be prescribed. The dosage begins at 5 mg. daily by mouth, starting during the sixth or seventh week (counting from the first day of the last menstrual period). The daily dosage is increased by 5 mg. every two weeks until the fifteenth week, when 25 mg. daily is given. Thereafter the daily dosage is increased by 5 mg. each week. Administration is discontinued at the end of the thirty-fifth week, since a drop in oestrogen and progesterone normally precedes the onset of labour.

Limitation of activity at the missed period times must be insisted on, and defaecation should be controlled by the use of mild aperients. Coitus must be avoided altogether.

Finally, there is much evidence for saying that there is a functional factor in cases of habitual abortion which may be largely responsible for subsequent miscarriages. It is most important therefore to reassure the patient that she still has a chance of reaching full term. The elaborate treatment so often given to these patients may be a potent factor in increasing confidence, thus promoting the chance of a successful delivery.

Next Refresher Course Article.—"Tachycardia," by Professor Crighton Bramwell.

Nova et Vetera

VESALIUS ON THE HUMAN BRAIN

Vesalius on the Human Brain. Edited and Translated by Charles Singer. (Pp. 151. £1 1s.) Published for the Wellcome Historical Medical Museum by Geoffrey Cumberlege (Oxford University Press). 1952.

This is the first book to contain a translation into English of any substantial part of that truly epoch-making work on anatomy, the *Fabrica* of Vesalius, originally printed at Basle in 1543. It was the first great work of science in the modern manner, the first to adapt exact graphic treatment to biological research, and the first to introduce a positive basis into medical education. Professor Singer has chosen the section on the brain because it is probably the most mature section of the work of Vesalius and because it illustrates the trend of medical thought at the time, prior to the work of Harvey.

There can be no doubt that the *Fabrica* depended for its success on the magnificent illustrations, more accurate than any before them except those of Leonardo, who failed to publish his researches. The drawings have a remarkable dynamic quality, and they surpass those of Calcar, who drew the illustrations for the earlier work of Vesalius, called *Tabulae Sex* and dated 1538. Professor Singer does not think that Calcar was the artist of the *Fabrica*. The letterpress in its original Latin, which the translator stigmatizes as vast, verbose, clumsy, and ill-chosen, is greatly inferior to the drawings. Nevertheless this was the best account of the brain of that time and for several generations to follow, based as it was upon observation and not on tradition. Professor Singer gives some valuable notes on previous anatomical work, and he shows how Vesalius, in dissecting the brain, followed the method he had learned in Paris. Anatomists, historians, and others may well feel grateful to Professor Singer for providing a translation of this important part of a medical classic which exercised so profound an influence on the progress of medicine.

DOUGLAS GUTHRIE.

THE HUNTERIAN BIRTHDAY ORATION

Twenty years after John Hunter's death Matthew Baillie and Sir Everard Home arranged for the delivery of an annual oration on his birthday, February 13. The latest in the long succession of orators was Mr. L. E. C. Norbury, who, before the Royal College of Surgeons the other evening, gave a discourse in which he managed to throw a kindlier light on Hunter's character than has been current in recent times. He described Hunter as emotional and quickly moved to sympathy, and with a sense of humour which came out particularly in letters to his brother William and others. Some people had a notion that Hunter's marriage was unhappy, perhaps because of the often published story of his irritation at his wife's taste for fashionable society. Hunter married Anne Home in 1771; she was 29 at the time and he was 43. She was a charming lady, and talented, too—did she not write the lines beginning "My mother bids me bind my hair"?—and she was, moreover, a good wife, devoted to her husband, and Hunter had the felicity of matrimonial success.

Mr. Norbury described Hunter as a great experimenter and observer and a great thinker above all. He read from Nature and took his science from no other source. An indefatigable worker, he was never satisfied until he thought his observations were correct. Observing many things, he tried to press a great deal into little, which perhaps was the reason for his defects as a lecturer. He was himself conscious of the difficulty of making others understand what seemed simple to himself. His writings were extensive, his first published work being a treatise on the natural history of the human teeth, dated 1771.

The lecturer concluded with a glance at some of Hunter's great contemporaries. A great legacy which Hunter left to posterity was his museum, but greater still was the spirit and tradition which had animated his disciples.

Hunterian Festival Dinner

A few hours after the Oration a large company of guests assembled at the invitation of the Royal College of Surgeons for the Hunterian Festival Dinner at the College. Mr. Iain Macleod, the Minister of Health, proposing the toast to "The College," said that since the days of John Hunter British surgery had led the world; in particular, British surgeons had been pre-eminent in operations on the lungs, heart, and brain, and in plastic surgery. Developments in the science of anaesthesia had been as splendid in this country as anywhere in the world. The great tradition of the College in research and education would certainly endure.

In response, Sir Cecil Wakeley reviewed the activities of the College and described the impressive progress that was being made with the building of the new College. The Queen, an Honorary Fellow of the College, would lay the memorial stone of the new buildings on May 5. The President also announced that the Duke of Edinburgh had accepted an Honorary Fellowship of the College, and would come to the College to receive it later in the year. Among the research activities of the College Sir Cecil mentioned particularly the new department of pharmacology which was coming into being, thanks to the generosity and interest of certain pharmaceutical firms; Imperial Chemical Industries, Limited, had agreed to finance the department to the extent of £10,000 per annum for the next seven years. The museum was about to benefit from a new trust fund—the Macrae-Webb-Johnson Fund. Lady Webb-Johnson had joined her husband as a college benefactor by making over a fund worth about £1,000 a year, to be used for the benefit of the museum on the advice of the Hunterian Trustees. This gift was made to commemorate her father and as a tribute to her husband's presidency of the College.

Sir James Paterson Ross had the formidable task of proposing the health of the many distinguished guests. After Sir Denys Lowson had replied for the guests, Sir Reginald Watson-Jones proposed the toast to the Hunterian Orator, Mr. L. E. C. Norbury, who made a brief response.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

The Metric System

SIR,—The metric system is rather like the sea serpent in that it gives rise to periodical discussion in which feelings run high. Like many other "tidy" plans, it looks admirable on paper, but actually bristles with difficulties when applied to medicine. In the first place, Professor W. C. W. Nixon and Mr. T. D. Whittet (February 7, p. 327) are not really advocating the metric system at all but the "international system of weights and measures," and this is full of anomalies. For example, a purist will hold up his hands in horror if you talk about cubic centimetres, but if you ask him what his red blood count is he will say five million per cubic millimetre. I happen to be partly responsible for the publication of a quarterly journal, and the history of this very minor matter is instructive. Some time ago we were solemnly admonished by some semi-official body, whose name I have forgotten, that it was very wrong to use c.c. and c.cs. for the singular and plural of cubic centimetres, and that the correct abbreviation was c.cm. for both. We had just got our compositors clear on this, when another notice arrived, saying that, as cubic centimetres were not a measure of volume, the correct designation was millilitres abbreviated to ml. Once bitten twice shy, and we did nothing, which was just as well, as the abbreviation was next altered to mil., which at least had the advantage of being a word in its own right. Alas, this has also gone with the wind, and we are now back at ml. Our journal now rests on the conservative platform of c.cm. This type of meddling is not only exasperating but is exploited by manufacturers. For example, the makers of one type of syringe advertised its advantage by saying that it was calibrated in millilitres instead of cubic centimetres. I believe that a syringe would have to be of at least two litres capacity to detect any difference at all.

The change-over to the new system would not be so easy as the authors suppose. They have pointed out the dangers of misplacing decimal points, but there is much more to it than this. A good deal of the method of memorizing doses is built up on the avoirdupois system, and all sorts of difficulties would arise. For example, any houseman knows that the usual pre-operative rectal dose of paraldehyde is 1 drachm per stone body weight, but is he going to remember it as 3.55 ml. per 6.35 kg.? If the change is to be made at all, it would have to be complete, and medical literature will be still further divorced from that of everyday life. How many people could visualize a patient 1.895 metres high weighing 64.37 kg.?

To avoid this kind of thing, agreement would have to be reached in the medical, scientific, and industrial worlds of the English-speaking nations. There is no prospect of this in the foreseeable future. For example, the last time this subject was discussed at the Engineering Section of the British Association members could not even agree that the change is desirable, let alone practicable. The view was freely expressed that, as in many fields production by Anglo-Saxon countries was greater than that of the rest of the world put together, it was unreasonable to expect the vast effort of changing over to be made. An American closed the discussion with the trenchant summary, "Your metre, my foot."—I am, etc.,

London, E.C.1. C. LANGTON HEWER.

Emphysema

SIR,—Dr. J. Todd's letter (January 24, p. 219) puzzles me. He criticizes me because I "made no attempt to define the clinical criteria which would enable the practitioner to decide which of these cases could be given morphine with

'safe and useful' results," yet I thought my letter made it quite clear that I was asking for just that guidance. I doubt if any G.P. has enough experience and knowledge to supply it, but I did hope that possibly the author of "the erudite address," which I obviously appreciated, could do so.

Our problem may be illustrated by the example Dr. Todd offers. It is, of course, conceivable that all our cases of status asthmaticus which have benefited by morphine have really been attacks of cardiac asthma in our chronic asthmatics, but, if so, how are we to tell? Incidentally, the cough reflex he mentions is not of first importance in a man gasping for his life, but the factors I mentioned—"anxiety, distress, and the demand of the tissues for oxygen"—most certainly are. It is incontestable that vastly more lives have been saved in general practice by the use of morphine than by withholding it, and one main object of my letter was to find out how to avoid using it in dangerous cases.

We must remember that conditions in hospital are not the same as in general, especially country, practice, but it is certainly wrong to condemn potentially life-saving treatment just because it has potential dangers. The task of medicine remains, as I said in my first letter, not to damn but to define "when it is safe and useful and when it is not," and it requires much experience as well as great erudition to do so.—I am, etc.,

Winsford, Cheshire. W. N. LEAK.

Parenteral Treatment of Crushed Abdomen

SIR,—The object of this case report is to show how modern intravenous treatment may keep both fluid and biochemical balance over a long period. Facilities for blood analysis are the only special ones necessary.

A 19-year-old man, weighing 8 st. 8 lb. (54 kg.), was crushed between two heavy vehicles. He was in a state of shock and showed signs that were those of either a ruptured gut or intra-abdominal haemorrhage. He had also a contusion of the right lung and heart. Laparotomy revealed a deeply lacerated liver that was repaired and a retroperitoneal haematoma of the right colon. On the 11th day a burst abdomen was found to be due to the effects of traumatic pancreatitis. On the 20th day a duodenal fistula appeared in the wound and persisted. Thereafter residual abscesses declared themselves by spontaneous discharge through the fistula and by discharge through a right loin incision made for that purpose. Until the 65th day his evening temperature averaged 102° F. (38.9° C.) and pulse 120. On the 65th day a painful abdominal episode associated with distension was accompanied by a sudden cessation of fever. This indicated that his major residual abscess had discharged into the gut. Then he was much improved, and recovery has since been complete.

Management was based on clinical observation assisted by accurate fluid charts and blood analyses for biochemical and haematological information. Intravenous management was particularly important in the first 19 days, when 65 pints (36.92 l.) of fluid were removed from his stomach by hourly suction. During this time intravenous fluids amounted to 115 pints (65.32 l.). This consisted of calculated quantities of Ringer's solution and combinations of glucose, saline, protein hydrolysate ("casydrol"), and blood. At this time he was balanced in fluid and salt. However, the protein had fallen to 6.3 g.% with an A/G reversal and the potassium to 15 mg. per 100 ml. The CO_2-combining power was 75 volumes %.

From the 20th to the 26th day the duodenal fistula discharged copiously. Having forgone solid food for three weeks, it was considered necessary tentatively to introduce protein and salts by mouth. This, with intermittent stomach suction and continuous fistula suction, was augmented by repeated intravenous drips that included Darrow's and Ringer's solutions. By the 30th day the fistula was practically dry. There had developed, however, an alkalosis, indicated by 79 volumes % CO_2 combining power and a blood salt reduced to 480 mg. per 100 ml. The potassium meanwhile had improved to 17 mg. %. Subsequently the diet was supplemented by potassium chloride cachets of 1 g. daily and deliberate salt consumption by the patient. It was noted how chloride continued in the urine in spite of a depleted blood salt while the alkalosis remained. Thus blood samples were essential for chloride estimation. Protein hydrolysate intravenously and by mouth assisted the recovery of the plasma protein. By the 35th day the patient's blood chemistry was normal apart from a slightly reduced plasma protein, and he was taking increasing quantities of light diet. Until the 65th day his weight remained the same at 6 st. 12 lb. (43.2 kg.) in spite of the continued fever. During this period transfusions were also administered at about fortnightly intervals to restore his haemoglobin from 60% to 75% on each occasion. The co-operation of the patient in taking all necessary dietary supplements was achieved by keeping him informed of his requirements. Thus his nutrition remained virtually balanced for nine weeks with intravenous administrations and a small diet.

Grateful acknowledgments are due to Mr. J. H. Conyers for his encouragement in treating this young man. For the careful attention that resulted in his recovery they are due in particular to Captain Smith and Sister Lester of the Military Hospital, York.—I am, etc.,

Manchester, 6. STEVENS DIMANT.

Bathing and Vestibular Palsy due to Streptomycin

SIR,—May I raise the question of the behaviour under water of the children who were treated in the earlier post-war years with streptomycin for tuberculous meningitis, and who may be making their first ventures into a medium entirely new, constituting a special predicament for them, denuded as they invariably are of vestibular sensation? My own belief, based on otoneurological observations at the time, is that few, if any, will have recovered from this selective paralysis, and a pronouncement by more recent workers is desirable as to whether complete immersion during swimming and diving may prove a hazard. Ordinarily, the direction of light penetration and water-pressure at body surface will be aids to orientation, but young children with bilateral vestibular palsy may be expected to panic or even drown if unattended.

I would remind physicians who have had the immense satisfaction of delivering these children from a previously fatal disease at so relatively small a cost in terms of sequelae that successful performance of the ordinary clinical neurological tests of balance can cover gross vestibular defect; they may wish to advise school health services of cases where recovery of specific vestibular function has not been established.—I am, etc.,

Bramhall, Cheshire. H. C. PURCER SMITH.

Use of Succinylcholine in E.C.T.

SIR,—We have read the article on the use of succinylcholine in E.C.T. by Drs. D. J. Adderley and Max Hamilton (January 24, p. 195) with much interest. We should, however, like to suggest that the rise in blood pressure following the injection of succinylcholine is not due to the drug but to the fact that the patient was ventilated with a mixture of 5% carbon dioxide in oxygen. This mixture, with or without efficient ventilation in an apnoeic subject, could easily produce a carbon dioxide build-up, the effect of which has been long known to cause an increase in blood pressure at least as high as that recorded in the article.—We are, etc.,

J. A. SMITH.
London, W.12. F. G. WOOD-SMITH.

Relationship of the Suprarenal Cortex to the Differentiation of Chromaffin Cells

SIR,—As a result of our studies in several species of animals, we reported in 1951[1] that the amounts of *nor*adrenaline and adrenaline found in the suprarenal glands seemed to bear some relationship to the relative size of the cortex. In the rabbit and guinea-pig (where the cortex is large relative to the medulla), methylation of *nor*adrenaline to form adrenaline is almost complete, whilst in the whale and fowl (where the medulla is relatively large) only a small amount of adrenaline is found. It was suggested that the cortex might be intimately concerned with methylation of *nor*-adrenaline.

Further work indicates that methylation can occur even in the absence of intimate relation with the cortex. Both adren-

aline and *nor*adrenaline have been detected, for example, in the rudimentary suprarenal medulla of the dogfish,[3] and in the organs of Zuckerkandl in children aged 6 months or more,[3] although both these structures are quite separate from cortical tissue. In our view there is no convincing evidence to connect the functions of the cortex with those of the medulla, though it is possible that cortical hormones may affect the degree of methylation in these chromaffin structures via the blood supply.—I am, etc.,

Dundee. G. B. WEST.

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Soft-tissue Radiology

SIR,—I have read with interest your annotation on "Soft-tissue Radiology" (January 10, p. 89), with its survey of technical advances in this field. I notice that mention is made of the problem posed by the fact that *x* rays are absorbed by soft tissues to a uniform degree. I therefore expected to find some mention of the late A. E. Barclay's work in this respect,[1 2] but was disappointed. His micro-radiology, a direct and more practical advance from the technique of Lamarque,[3] should, I feel, receive especial mention in any discussion of soft-tissue radiology, for the technique has much to offer in many fields of medical and biological research.—I am, etc.,

Crawley, Sussex. DONALD LEATHERDALE.

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[2] *Microarteriography*, 1951. Blackwell, Oxford.
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Measurement of Tissue Components Radiologically

SIR,—Dr. Frank Falkner and Miss Sylvia Wisdom (January 31, p. 275) did not need the tube-plate distance or object-plate distance in order to find the length of the object, because they already had the tube-shift, image-shift, and length of image. Their graph was unnecessary, therefore. Thus: O=object, I=image, TS=tube-shift, IS=image-shift.

$$O = I \times \frac{TS}{TS + IS}$$

In their formula $\frac{K-d}{K}$ is the same as $\frac{TS}{TS + IS}$

This is the formula for a length parallel to plate and plane of source of rays. It is of little use for an irregular object. I imagine it would be better to abandon calculation and instead to reproduce to scale the triangles in question, and in that way find by direct measurement the limits of the dimensions of the object.—I am, etc.,

Heath Hayes, Staffs. P. J. O'BRIEN.

The General Practitioner and Mass Radiography

SIR,—It may interest you and your readers to know that in August last the North-west Metropolitan Regional Hospital Board set up a mass *x*-ray unit at the Central Middlesex Hospital as an extension of the radiological services provided by it, with the primary object of carrying out an investigation into the incidence of unsuspected chest disease in the patients attending or admitted to the hospital. It was found possible to extend the mass radiographic facilities to general practitioners in the surrounding area. Practitioners are able to refer patients direct to the mass radiography department on any weekday within normal working hours without appointment. A member of the radiological staff reports on the films within 24 hours, and a negative report is received by the practitioner within three days of the patient attending. If the report indicates suspicions of disease a large film is taken, and any of the further necessary radiological investigation is carried out in the main *x*-ray department and a subsequent report sent to the practitioner. Should a diagnosis of active, or possibly active, tuberculous disease be made, the chest physician of the area in which the patient lives is informed at the same time as the patient's general practitioner.

It is intended to publish an account of the experience gained in this scheme after a trial period of approximately a year. So far, out of the comparatively small number of 1,431 patients referred by general practitioners, 21 have had active, or possibly active, pulmonary tuberculosis, and five patients have been diagnosed as suffering from neoplasm of the lungs. It is not intended in this letter to do more than draw attention to the fact that the opportunity referred to in the final paragraph of your annotation (February 7, p. 322) has already been taken, and that in at least one area the radiological services have been extended even a stage further than that described in the very interesting article by Dr. F. A. Nash, Mr. B. Benjamin, and Dr. T. J. Lee (p. 304).—I am, etc.,

London, N.W.10. F. PYGOTT.

SIR,—I would like to congratulate Dr. F. A. Nash and his colleagues on an excellent piece of work (February 7, p. 304), which will focus attention once more on the ever-present need for the early diagnosis of pulmonary tuberculosis. The suggestion that the services of the mass radiography unit should be employed in this fashion, however, is both impracticable and dangerous, and if adopted would constitute a disservice to the anti-tuberculosis campaign.

While it is not my purpose to attempt to devalue an excellent paper, I am struck by the relatively small number of patients attending for the first time at the chest clinics in the survey area (less than one-third the number in my own area of similar population). It is also clear that the number of patients *x*-rayed falls far short of the estimated needed requirements. The authors refer to the work of Toussaint, but do not mention that schemes similar to their own on a comparable scale are a common feature of many chest clinics. It is my opinion that the chest physician is best fitted to control the attack on tuberculosis. So far as diagnosis is concerned, this should be effected by a harmonious co-operation between general practitioner and chest physician. A split in the tuberculosis service between diagnosis, treatment, and prevention and aftercare has already been imposed from above, to the detriment of the patient. Let us take care that a further split does not arise, this time of our own making.—I am, etc.,

Wrexham. E. CLIFFORD-JONES.

Reprints of Communications on Stress and the Adaptive Hormones

SIR,—In perusing the current literature with which your *Journal* is concerned, we note that an ever-increasing number of its articles deal with problems pertaining to research on "stress" and the so-called "adaptive hormones" (A.C.T.H., S.T.H., corticoids, adrenergic substances, etc.). We are writing to you because, in our opinion, the success of research in this complex and rapidly developing field largely depends upon the prompt availability and evaluation of relevant publications, a task for which we should like to solicit the assistance of your readers.

In 1950 our Institute initiated the publication of a series of reference volumes entitled *Annual Reports on Stress* (Acta Medical Publishers, Montreal) in which the entire current world literature is surveyed every year (usually between 2,000 and 4,000 publications). Up to now we had to compile the pertinent literature partly from medical periodicals, monographs, abstract journals, and partly from reprints sent to us by the authors themselves. Of all these, reprints proved to be the best source of data which we felt deserved prompt attention in our annual reports. Hence, in the past, we have sent out several thousand individual reprint requests to authors whom we knew to be engaged currently in research on stress and allied topics. Even this procedure did not give us the wide coverage which would

be desirable, because it is materially impossible to contact all these authors individually, and it often takes too much time to get the requested reprints.

It is evident that in order to ensure prompt inclusion of publications in the annual reports these surveys must develop into a co-operative effort between the authors of original papers and the reviewers. This co-operation was greatly enhanced of late by the publication of announcements, in several medical journals, encouraging investigators interested in stress research to send us their reprints for this purpose as soon as they become available. We should be grateful if, by the publication of this note, you would also bring this problem to the attention of your readers.—We are, etc.,

HANS SELYE,
Professor and Director of the Institute of Experimental Medicine and Surgery.

University of Montreal, Montreal, Canada.

ALEXANDER HORAVA,
Co-author, *Annual Reports on Stress*.

"Pasteur's Flask" in Sydney University

SIR,—I wish to thank Dr. Lilian A. Bates for her interesting letter (November 1, 1952, p. 993) concerning the flask of bouillon or beef broth which was brought to Sydney from the Pasteur Institute in Paris in 1888. I regret my error in stating (August 23, 1952, p. 439) that the flask of broth was put up by Pasteur himself. The association interest remains, however, because, although Pasteur did not put up the flask himself, it was prepared by his nephew, Dr. Adrien Loir, in Pasteur's laboratory on Pasteur's instructions. Madame Pasteur, it appears, also came into the story, because it was her scrutiny of *Le Temps* which brought the need of the Government of New South Wales under the notice of her husband.

Sydney students will still regard the Pasteur flask as a precious exhibit, because it is one of the few links our museum provides with France, a country which has made outstanding contributions to the welfare of mankind. This flask, because of its associations, will continue to remind us of one of the noblest sons of France, Louis Pasteur, whose life and work are an inspiration to students in every land.—I am, etc.,

Sydney. KEITH INGLIS.

Misuse of Words

SIR,—As a critic of the usage of words, is not Professor A. G. Watkins (February 7, p. 335) himself in error? Since "gynaecological" means "concerning the science of diseases of women," is it the medical student or the patient who undergoes a gynaecological examination? Similarly, since "pathological" means "concerning the science of disease," it is surely nice usage when this adjective is applied to a department.—I am, etc.,

London, S.W.10. M. J. PURDY.

Quintuple Pregnancy

SIR,—The birth of quintuplets is still an obstetrical rarity, and it is thought that the following notes of the general practitioner's antenatal findings in such a case may be of interest.

The mother, aged 36, had previously had five full-term single pregnancies. All these births had taken place in hospital, and her last baby, now aged 6, weighed 9½ lb. (4.3 kg.) at birth. She was first seen in the pregnancy which is the subject of this report on August 25, 1952, being then about 12 weeks pregnant. Apart from varicose veins of both legs there was nothing abnormal in her condition. She was next seen on November 17, when one foetal heart was heard. The blood pressure was 120/80, and no abnormality in size or condition was noted.

The patient did not present herself for examination, as requested, in December, and she was next seen on January 6, 1953. The changes which had occurred were quite alarming. The abdomen was greatly distended, and at the twenty-eighth week appeared to be at full-term. There was a gain in weight of 15 lb. (6.75 kg.). A foetal heart was heard in the left sacro-anterior foetal position. The blood pressure was elevated to 150/80, and there was moderate oedema of both legs and ankles, but no undue distress. On examination the uterus was tense, as with hydramnios; no foetal movements were felt. Palpation revealed the presence of many small hard protruding lumps, especially on the right side of the uterus. This would have been consistent with the presence of multiple small intramural fibroids. The urine was free of frank albumin, but the Bence Jones reaction was present.

A diagnosis of multiple pregnancy was made, with an alternative diagnosis of breech presentation and multiple small uterine fibroids. The patient was referred to hospital, where macerated male quintuplets were born nine days later within the space of three hours.—I am, etc.,

Herne Bay, Kent. P. DE B. RANSOME-WALLIS.

Intraperitoneal Rupture of Rectovaginal Abscess Due to Proctotomy

SIR,—Although the weight of present-day opinion is in general against proctotomy for abscess in the rectovaginal or rectovesical pouch, the procedure is still occasionally recommended by writers on the subject, and rare cases occur in practice in which it seems the obvious treatment. To the numerous objections advanced we have to add another unfortunate accident.

The patient, a female aged 17 years, had an acutely inflamed unruptured appendix removed and the abdomen closed without drainage. She thereafter developed signs of a residual abscess, which was eventually located in the pouch of Douglas. In view of the degree of toxaemia, it was thought best to open this rather than wait for spontaneous evacuation per rectum. Incision was carried out under a general anaesthetic 15 days after her original operation. Only a small amount of pus was obtained. Some hours later the general condition became much worse, and obviously some catastrophe had occurred. Sixteen hours after the proctotomy a simple laparotomy and drainage was performed. The abdomen was found full of pus. The patient died later in the same day.

It seems fairly certain that rupture of the abscess into the general peritoneal cavity was caused by the sudden increase of tension when the instrument was thrust into it from the rectum. This has doubtless occurred before, though we have found no record of it even among the stock objections to the operation. Rupture of adhesions due to the collapse of the cavity consequent upon drainage has been recorded,[1] but in such a case there would be a profuse flow of pus first. Spontaneous rupture in both directions has also been mentioned by the same author; presumably it was also simultaneous.—We are, etc.,

R. D. N. BISSET.
Salisbury. A. DUFF.

[1] Vale, C. F., *Ann. Surg.*, 1940, 111, 396.

The Climacteric

SIR,—With reference to your timely annotation on "The Climacteric and Oestrogen Therapy" (January 3, p. 37), the following additional psychological aspect of climacteric disturbance needs to be more widely appreciated. The psychological reaction both to increasing age and temporary enhancement of inner tensions are sharper in those women whose cultural achievement has been severely limited; this applies to women of various social status and otherwise different personality background. Where a woman's life has previously centred almost exclusively about her domestic, motherhood, and sexual functions without any consolidated outer interests, the increasing independence of the children and the changing body image serve to evoke feelings of loss and anxiety which are especially threatening because there are no available compensations which can be more energetically utilized. In "minor" psychotherapy it is necessary to encourage the evolution of interests outside the home and to engage the attention of available social agencies so that they can help with this problem. This is

especially the job of the general practitioner, and in giving this aspect of treatment his serious attention involutional trouble can be averted in many cases. Of course, in some with, for example, severe obsessional character disorder and a good deal of inward guilt and tension in their personality background such "minor" psychotherapy would not be sufficient. But I feel that attention directed towards the change in the life situation of the patient in discussion with her usual physician is a very important therapeutic and prophylactic measure. Especially in the culturally restricted woman, the feeling that life has at this stage of the game lost its value, and she hers, is one to be energetically countered by her medical adviser.—I am, etc.,

Chapel Hill, North Carolina. D. W. ABSE.

Abuse of Antibiotics

SIR,—I agree entirely with Mr. Norman Lake's letter on abuse of antibiotics (December 13, 1952, p. 1307), but I am writing to express my surprise that he reports without comment the case in which a perforated appendix was left *in situ* in the presence of generalized peritonitis. I am not surprised to learn that the patient's peritoneum was found to be full of pus at the second operation; on the contrary I would have been very surprised indeed if this had not occurred. Drainage alone in a case of perforation of the appendix is permissible only when a localized abscess is present. In a case in which generalized peritonitis is diagnosed at or before operation the appendix must be removed. Once this is done drainage is of comparatively secondary importance now that we have efficient antibiotic agents; but the actual removal of the offending appendix is absolutely essential to prevent the continuation of infection of the peritoneum.

This letter is not written in order just to criticize the management of the above case (there are, of course, possible exceptions to every rule in medicine), but to be a reminder and a warning to the more junior and less experienced surgeons, and to prevent them from adopting drainage without appendicectomy as the correct treatment of generalized peritonitis due to a perforated appendix.—I am, etc.,

Georgetown, British Guiana. N. N. IOVETZ-TERESHCHENKO.

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The Dangers of Blood Transfusion

SIR—The article on the -D-/-D- genotype (January 24, p. 198) attracted my attention merely because of the name of one of the co-authors, Dr. Ruth Sanger, whom I was glad to have seated at my table on one of my transatlantic voyages. Other readers, like myself, may find this article beyond their complete comprehension, and without the personal contact might pass it by. However, do not these highly technical articles on blood emphasize what a dangerous treatment transfusion may be? Frequent discoveries of antibodies and genotypes not previously suspected should make one wary of administering blood except as an urgent necessity. The great number of transfusions now being given on one pretext or another must enormously increase the risk of conflicting antibodies endangering life when a subsequent transfusion may be a necessity.

Statistics seem to prove that there is an immediate advantage in using whole blood, but, in view of the highly technical and skilful investigations which constantly are discovering potential dangers and which are demonstrated to us by complicated formulae, ought we not to regard a transfusion of blood, not as a routine measure, but as a dangerous major operation? The Christian pronouncement of nearly 2,000 years ago, "It is more blessed to give than to receive," may well be true as regards the giving and receiving of blood. The recipient, perhaps, is being conditioned for future unknown dangers—but what of the donor? The generous donor is willing to give blood to "save life," but I do not think that gallons of this precious and dangerous fluid should be wasted as a routine administration in operative technique. If a pint of blood is essential for recovery, or merely the more rapid recovery, of the patient, then surely the blood cannot be obtained from the donor without cost? Wolstein said in 1791, when condemning blood-letting, the fashion of his day, "Blood is no water—it is the juice of life; a juice which after each venesection Nature replaces rapidly, but in a raw, unprepared, watery, spiritless state." We have learned much about "the juice of life" since Wolstein's day, but no doubt his clinical observation was correct, as also that of Marshall Hall, who denounced the same practice, calling the lancet "a minute instrument of mighty mischief." Some time ago when doing a short locum for a friend I saw two patients, man and wife, labelled as suffering from rheumatism. Neither had ever had any serious illness, but each appeared to be debilitated and only very slowly convalescing. They complained of great tiredness and lack of energy and indefinite aches and pains, which evidently suggested the "diagnosis" of rheumatism. They said that neither had felt well since their last donation of blood. They were universal donors and both had been called upon, and had responded willingly, many times.

I am not satisfied that the sacrifice of the donor is as harmless as is generally supposed, nor am I satisfied that a transfusion is always a good thing for the recipient. I would only submit myself and members of my own family to a transfusion if I considered it an absolute necessity, and this must be the criterion for my patients. What can I tell the would-be donors who ask my advice? I do not wish to discourage them, nor do I wish to embarrass the workers in the blood-collecting squad, but I do feel that it is time we exercised extreme economy in the use of blood, other persons' blood, and ensure that it is used only for the purpose for which most persons think they give it—to save life.—I am, etc.,

Huddersfield. S. H. WADDY.

Treatment of Bowel Infections of the Tropics

SIR,—I would like to express disagreement with a statement made in Dr. A. R. D. Adams's article on bowel infections in the Tropics (February 7, p. 308). He says: "While emetine will unfailingly bring an acute attack of amoebic dysentery rapidly to an end, usually it will not sterilize the bowel of the infection, however unwisely the drug may be pushed or the course of treatment with it be prolonged." During the years 1942–4 I had in my care 363 cases of amoebic dysentery among British troops in India, and although the response to emetine was dramatic in most instances I encountered a number of patients who showed no response whatever. Some of these showed an immediate response to carbarsone given orally, and the history indicated that the disease had been contracted in North-east India. Conversely there were patients from the Madras district who failed to show any response to carbarsone but reacted at once to emetine. At that time carbarsone had a high reputation in Calcutta, and one wonders whether "emetine-resistant" and "carbarsone-resistant" strains exist in India and whether Dr. Adams has been fortunate enough to work only in an area where the amoebae were "emetine-sensitive." I had hoped to gather some accurate information on the subject, but we had only just become aware of the possibility when the hospital in which I was working moved elsewhere and the unofficial "dysentery unit" ceased to exist.

Failure of emetine to sterilize the bowel, as Dr. Adams says, is well known, and the majority of the persistently relapsing cases had received treatment in the first instance of emetine only, sometimes only six injections being given. Once an adequate supply of chiniofone ("quinoxyl") became available and was given in a five-day course by mouth and as retention enemas, the obstinate relapsing cases became less frequent, and few cases who had had the full course came back as relapses. It would be interesting to know if other workers have found any evidence of strains of the entamoeba which can be differentiated therapeutically.—I am, etc.,

Keighley. IAN STEWART.

Half-circle Intestinal Clamps

SIR,—The spring clamp illustrated was originally devised for anterior resection of the rectum. It has also proved useful in intraperitoneal intestinal resection and even in oesophago-gastric or oesophago-jejunal anastomosis. The

depth of 2 in. (5 cm.) allows enough bowel to project for anastomosis, and the maximum diameter of 3½ in. (8.75 cm.) permits haemostasis and freedom of movement in an otherwise restricted space.

I am indebted to Messrs. Down Bros. for making this instrument for me.—I am, etc.,

London, S.E.1. GUY BLACKBURN.

Prevention and Treatment of Tetanus

SIR,—In my recent refresher course article on the prevention and treatment of tetanus (January 17, p. 150) I said that mephenesin ("myanesin") "may be given either intramuscularly or orally in doses of 0.5 to 1 g. for an adult, repeated every few hours according to the effect produced." The British Drug Houses, Ltd., comment on this as follows: "Myanesin is available for oral administration both in the form of elixir and tablets. We do not advocate the use of elixir by mouth in cases of tetanus, since myanesin possesses local anaesthetic properties, so that if the elixir is given to a case of tetanus in which dysphagia is present the local anaesthetic effect may result in abolition of the swallowing reflex with the consequent aspiration of foreign material into the trachea and lungs. The administration of myanesin tablets does not give rise to the local anaesthetic effect on the palate and pharynx, but, on the other hand, we have no records of its therapeutic efficacy in tetanus. According to our records the most satisfactory method of administering myanesin in cases of tetanus is by intramuscular injection." I think this observation is important.

Dr. L. H. Cane (February 14, p. 403) asks a pertinent question regarding the dosage of International Units for passive immunization. As he states, the 1950 I.U. is twice the potency of the 1928 I.U. Throughout the article both for immunization and treatment the dosage was expressed in 1928 I.U. It would have been more correctly and clearly expressed in 1950 I.U., the figures "1950" being added for clarity.

The question of negligence and blame for failing to give a prophylactic injection of antitoxin to a patient who subsequently develops tetanus is a very difficult one. Each case must be judged on its merits, and the types of wound enumerated which are known to have caused the disease only serve as a general guide and warning. It may be some help to remember that wounds which have never been properly cleaned but have been allowed to scab over while dirty appear more prone to harbour the organism. In my opinion whitlows in those working in earth or manure do merit antitoxin, but it is manifestly impossible and inadvisable to give prophylactic antitoxin after every trivial wound, and therein lies the chief reason for failure of the method of passive immunization to afford complete protection to the community. The degree of natural resistance in man depends on many factors and is extremely difficult to assess.

Dr. R. G. Abercrombie (February 14, p. 403) raises the difficult problem of the danger of active surgical treatment to the wound after tetanus has declared itself. In my article I emphasized the importance of minimum disturbance of tissues after a large dose of antitoxin had been given. I agree that the stress should be on the "minimum," and nothing should be done until *after* antitoxin has been given, but with these reservations it would appear rational to try to prevent the continued production of toxin locally. I have never observed harmful effects from such limited interference, but admittedly this statement applies to patients with comparatively slight wounds. Owing to the increasing use of antitoxin in the 1914–18 war, tetanus following serious wounds in those who had not been passively immunized must have been comparatively rare after the first few months. Similarly in civilian patients they are exactly the cases to which prophylactic antitoxin is almost always given, and in the 1939–45 war tetanus was almost unknown. I have seen no example of this type from which to judge the effects of surgery. On the other hand, I have seen several on whom no surgical treatment was practised who died in spite of enormous doses of antitoxin. The answers to such questions depend a little on the definition of the word "severe" as applied to tetanus. It is only by the application of the prognostic criteria I outlined to a large number of cases that the relative values of different methods of treatment can be assessed.—I am, etc.,

Cambridge. LESLIE COLE.

Sensitization to Local Application of an Antihistamine

SIR,—Nowadays, when ready resort is made to the various antihistamines by mouth for a variety of allergies and hypersensitive reactions, it may not be readily realized that hypersensitivity may develop to antihistamine substances themselves when applied locally in the form of ointments. The following case illustrates well this seeming paradox.

The patient developed eczema of the hands and arms in 1949. The usual ointments were applied and each produced a temporary slight improvement. In July, 1952, he was given mepyramine maleate ("anthisan") by mouth, 100 mg. three times a day for 12 days, with no improvement. On September 1 phenindamine hydrogen tartrate ("thephorin") ointment was applied and produced a dramatic improvement. On October 18 he developed impetigo of the face, which failed to respond to gentian violet. Eleven days later his face had shown little improvement, and his hands gradually became oedematous, with exfoliation of the skin of the fingers. Phenindamine hydrogen tartrate ointment and gentian violet were discontinued. Mepyramine maleate, two tablets three times a day, was given, and acriflavine emulsion was applied to the face. The oedema of the hands quickly subsided and the impetigo of the face quickly disappeared. On November 15 an eczematous rash of hands and arms reappeared, and the effect of applying phenindamine hydrogen tartrate ointment was again tried. The oedema appeared as dramatically as before, with exudation of serous fluid, and again responded quickly when phenindamine hydrogen tartrate ointment was withheld and mepyramine maleate given by mouth. Since that time the hands have shown a steady improvement from the application of zinc and castor oil.

I reported this case to Roche Products Ltd., the manufacturers of thephorin ointment, asking if a constituent of the ointment base was the cause of the hypersensitivity. I received a reply from the medical adviser stating that this was unlikely and that it was much more probably caused by the thephorin itself, as other similar cases had occasionally been reported.

It seems strange that the cure of a disease should cause the disease itself.—I am, etc.,

Bristol. W. A. HEATON-WARD.

Medical Services for American Personnel

SIR,—It has been suggested by several British physicians, particularly those practising in the communities which are adjacent to United States bases in the United Kingdom, that information be circulated concerning the type of medical services available to American personnel and their dependants in the United Kingdom.

There are four U.S. Air Force hospitals in England: the 59th Medical Group located in Burtonwood, near Warrington, Lancs, serving the Liverpool region, telephone Warrington 3000, extensions 1070 or 1060; the 5th Hospital Group at Burderop Park, near Swindon, Wilts, serving

the Oxford area, telephone Wroughton 391; the 3rd Hospital Group at Wimpole Park, near Royston, Cambs, serving East Anglia, telephone Arrington 381; and the 494th Medical Group, serving the London area, telephone Waxlow 4300, extensions 112, 113, or 114. All of these hospitals have the following services and facilities available: general surgery, general medicine, ophthalmology, oto-rhino-laryngology, orthopaedics, paediatrics, obstetrics, gynaecology, out-patient, laboratory, pharmacy, and radiology. In order to provide the best type of specialized medical care, certain of these hospitals have been staffed and equipped over and above the others. Therefore in the case of difficult diagnostic problems covering the following specialties patients should be referred as indicated: neuropsychiatry—Burderop Park; urology—Burderop Park or South Ruislip; orthopaedics—Burderop Park; cardiology—South Ruislip; allergy—Wimpole Park; mortuary service—any hospitals listed or secure information from nearest American installation.

Should any British physician desire to use any of these facilities in his diagnosis or treatment of American patients, he may call on them direct or may ask the nearest hospital for assistance in securing consultation and transport facilities. *X*-ray examinations, all laboratory procedures, including basal metabolic rates, and electrocardiograms can be done. Prescriptions can be filled at all these and other medical establishments, such as infirmaries, although substitutes may be necessary where British and American medicines differ slightly.—I am, etc.,

L. R. BRASWELL,
Air Surgeon, Third U.S. Air Force.

Ruislip, Middlesex.

POINTS FROM LETTERS

Feeding of Babies

Dr. A. L. E. FILMER COLEMAN (Evesham) writes: I may be old and behind the times, but I am still convinced that if only we returned to starting babies off with three-hourly feeds, gradually lengthening the interval to four hours, we should not hear so much about this self-demand feeding. . . . Dr. J. Irene Rosie (January 31, p. 273) says, "The breast-feeding record is better in those babies who in the first 10 to 14 days of life are not kept on a too strict feeding régime." It is not the lack of strict régime; it is the fact that the mother, showing common sense, refuses to follow the, to my mind, silly and harmful four-hourly feeding.

"Prescribers' Notes"

Dr. F. E. S. HATFIELD (Chipping Ongar, Essex) writes: I have recently received a copy of *Prescribers' Notes*. I am fully in sympathy with the objects of this publication, but I feel that greater endeavours should be made to be objective. For instance, in this number a page is devoted to the drug "pregnenolone" which gives the impression that the drug is not only expensive but therapeutically valueless. In my experience—admittedly limited, as most general practitioners' experience of any one type of case must be—this drug gives symptomatic relief in most cases of active rheumatoid arthritis. I have had three cases in which a life of great suffering only made bearable by the constant ingestion of large quantities of tab. cod. co. was transformed by the drug. Unfortunately the symptoms relapse as soon as the drug is withdrawn, and in one case the dose had to be pushed to 10 tablets a day to get the full effect. In my opinion, rheumatoid arthritis is a disease which can cause so many years of prolonged suffering that any drug which promises relief should be fully utilized. It is common experience that costly drugs soon become cheaper if extensively used, and there has been at least one reduction of price in this case to my knowledge. If the reports in *Prescribers' Notes* are to be as biased on the one side as some of the reports of the less reputable drug firms are on the other, then it will certainly fail in its mission.

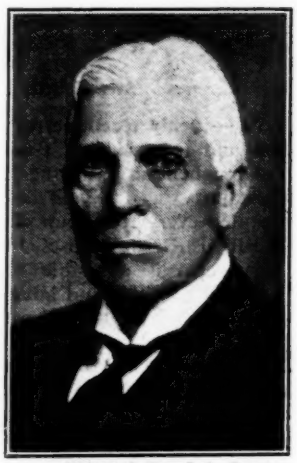
Second Attack of Chicken-pox

Dr. M. A. G. PIETRONI (Nicosia, Cyprus) writes: With reference to Dr. N. H. H. Golledge's letter (January 17, p. 163), I have personally witnessed undoubted second attacks of chicken-pox on two occasions. I have no records of the first case, but I observed in the second patient, now aged 7½, a definite though mild attack of chicken-pox in January, 1951, which lasted only a few days and which coincided with an epidemic at her school. Her second attack occurred in January of this year. This attack was profuse enough and will probably allow the little girl to build up her immunity.

Obituary

Sir HOLBURT WARING, BT., C.B.E.
M.S., F.R.C.S.

Sir Holburt Jacob Waring, who died at his home in Gloucestershire on February 10 at the age of 86, occupied an outstanding position in British surgery for many years. He had lived since the middle 'thirties in retirement at Tidenham in Gloucestershire, but many in London will vividly recall him not only as a surgeon of great eminence but as a dignified Vice-Chancellor of the University and a man of high capacity in administration in many public bodies. He never lost during his long career in the south his native Lancastrian abruptness of speech and manner, but those who got behind the manner to the man found a charming personality and a real friend.



[*Elliott & Fry, Ltd., London*

He was born on October 3, 1866, the son of Isaac Waring, of Southport, and was educated at Owens College, Manchester. He took his medical training at St. Bartholomew's, the hospital on whose staff he was to serve actively for thirty years. His university career was a brilliant one; he seemed to carry off all the prizes. He took the B.Sc.Lond. in 1888 with honours in physiology, the M.B. in 1890 with honours in medicine and forensic medicine, the B.S. in 1891 again with honours, and the M.S. in 1893, qualifying for the Gold Medal. His whole career was devoted to surgery. He became F.R.C.S. at the age of 25. In January, 1902, he was elected assistant surgeon at St. Bartholomew's, and full surgeon in 1909. He was also consulting surgeon to the Metropolitan Hospital, the Royal Dental Hospital, and to the Ministry of Pensions. His career was interrupted by service in the first European war, in which he held the rank of brevet-colonel R.A.M.C.(T.) and was mentioned in dispatches. Before the war he had served in the volunteer Medical Staff Corps and had transferred to the Territorial Force when it was established in 1908.

His election in 1932, in succession to Lord Moynihan, to the presidency of the Royal College of Surgeons of England, a position which he held for three years, was the crown of a long association with the Royal College in many capacities. In 1897–8 he was Erasmus Wilson lecturer, in 1921 Bradshaw lecturer, and in 1928 he delivered the Hunterian Oration. He was a trustee of the Hunterian Collection of the College and for 10 years a member of the Board of Examiners. He was also examiner in surgery for the universities of London, Oxford, and Manchester. In the University of London he had been Dean of the Faculty of Medicine and in 1922–4, at a time of important constitutional change in the University, he held the office of Vice-Chancellor. He was closely associated with the establishment of the London School of Hygiene and Tropical Medicine, and

the great institution in Gower Street owes much to his business ability in the chair of the Court of Governors and as its treasurer. For many years he was the representative of his university on the General Medical Council, and there and on the Dental Board, of both of which bodies he was treasurer, his business and financial ability proved of great service.

Waring was an able if somewhat formidable teacher, and the terseness of his style was well suited to the compilation of medical textbooks. His *Manual of Operative Surgery* was first published in 1892, when it consisted of 687 pages. In the sixth edition, published in 1927, the pages ran to nearly one thousand. In 1928 he published *The Surgical Treatment of Malignant Diseases.* An early work of his, published in 1897, was *Surgical Diseases of Liver, Gall Bladder, and Biliary System*, a dissertation on which subject had gained him the Jackson prize of the Royal College of Surgeons a few years before. He also contributed to many medical textbooks and periodicals. The articles on operations on the tongue and floor of the mouth in Burghard's *System of Operative Surgery* and on surgical disease of the pancreas in the *Encyclopaedia of Medicine and Surgery* were from his pen. With the late Sir D'Arcy Power he wrote a short history of St. Bartholomew's Hospital.

Among other leading positions which he occupied from time to time were those of president of the Medical Society of London in 1925–6, president of the Section of Surgery of the Royal Society of Medicine in 1928–30, treasurer of the Imperial Cancer Research Fund, vice-president of the Grand Council of the British Empire Cancer Campaign, and governor of East London College and of Christ's Hospital.

Waring was made C.B.E. at the close of his war service in 1919 and was knighted in 1925. In 1935 he was created a baronet "of St. Bartholomew's of the City of London." He was the recipient of honorary degrees of the Universities of Cairo and of Bristol and Durham, and was an honorary Fellow of the Royal Australasian College of Surgeons. He was also an officer of the Legion of Honour. Sir Holburt Waring, whose wife died in 1948, is survived by a son and two daughters.

We are indebted to Mr. J. BASIL HUME for the following appreciation: Holburt Waring, though never a very great surgeon, achieved distinction by a record of service in the profession which can rarely have been equalled. His offices, which included those of President of the Royal College of Surgeons, Vice-Chancellor of the University of London, and Chairman of the London School of Hygiene and Tropical Medicine, covered a wide field concerned with the co-ordination and advancement of medicine. With all this he never neglected what he considered to be his first duty—the care of patients at St. Bartholomew's. For thirty years he was a familiar figure in and about the hospital. The house-surgeons and dressers, all in clean white coats, awaited his arrival in the square. He was invariably punctual, and immediately led the way into the wards or the theatre. The dresser's notes were read and severely criticized, the patient was thoroughly examined, and a diagnosis or provisional diagnosis made. He hated indecision: his judgment was based on facts, and these when duly weighed made him firm and prompt in action. The great majority of his house-surgeons held him in high esteem and many in affection. They had to pass through the stage of being "the worst house-surgeon I have ever had" to be able to graduate to competence, but, that achieved, their interests were his.

In the same way Waring was sure of himself in matters of policy. The facts had been carefully ascertained and considered, and by his forceful speech and manner and skill in committee procedure he nearly always won his way. It is doubtful whether the new surgical block at Bart's would ever have been built if he had not forced the necessity for the building on governors and colleagues alike. Some were afraid of the cost, others that the square would be altered, but Waring had a conviction of future needs and developments that overcame all obstacles.

It is sad to recall that, with the loss of his friends Lockwood and Harrison Cripps, Waring became a very lonely man, plunging more and more actively into public affairs. That he lived to an advanced age with almost unimpaired mental powers is not remarkable when one considers the number of interests he maintained after his retirement. He came on the staff of Bart's in 1902, and is the last of the great men of the turn of the century.

W. H. GRACE, M.D., F.R.C.P.

Dr. W. H. Grace, who died at Chester on February 10 at the age of 60, was the Home Office pathologist for the north-western region from January, 1947, to March, 1952, when ill-health obliged him to resign from the appointment.

Walter Henry Grace was born in Australia on December 25, 1892, and, after graduating B.Sc. at the University of Sydney, he came to England to continue his medical studies at Guy's Hospital. He qualified M.R.C.S., L.R.C.P. in 1918 and took the degrees of M.B., B.S. of the University of London in the same year. After qualification he held a number of appointments at Guy's Hospital, including that of senior assistant bacteriologist, and then in 1922 he moved to Chester. Before leaving London he took the M.R.C.P. and the D.P.H., and in 1922 he proceeded to the degree of M.D. and took the D.T.M.&H. He was elected F.R.C.P. in 1939. At Chester Dr. Grace quickly made his mark as a pathologist of reliability, and his services were made full use of by the hospitals in the district. He became honorary pathologist and senior assistant physician at Chester Royal Infirmary, consulting pathologist to the Cheshire County Mental Hospital, and honorary pathologist to the Wrexham War Memorial Hospital and to Denbigh Infirmary. With the introduction of the National Health Service he was appointed consulting pathologist to the Chester group of hospitals. He was also part-time lecturer in forensic medicine and toxicology and examiner in forensic medicine at the University of Liverpool for some years. When the British Medical Association held its Annual Meeting at Liverpool in 1950 he served as a vice-president of the Section of Pathology and Bacteriology. On the establishment of the Chester and District Hospital Management Committee under the National Health Service in 1948 he was appointed vice-chairman, a position he held until 1952. He had also been chairman of the appointments subcommittee and vice-chairman of the staffing subcommittee.

As a Home Office pathologist Dr. Grace was often called on to give evidence in criminal prosecutions, and he appeared as an expert witness in the trial for murder of Dr. Buck Ruxton in 1936 and of Dr. R. G. Clements in 1947. As a witness his quiet, incisive voice commanded respect, and his answers to questions were uttered slowly and deliberately, without waste of words. By nature a cheerful, kindly man, he was most reluctant to give up much of his work last year, but ill-health made this inevitable. His memory will be cherished by his many friends.

Dr. GRIFFITH LLEWELYN JONES died at his home at Llangefni, Anglesey, on January 17 at the age of 80. He was born at Llanllyfni, Caernarvonshire, on October 25, 1872, and was educated at Denstone College, Uttoxeter, and St. Mungo's College, Glasgow. After obtaining the Scottish triple qualification in 1897 he was appointed house-surgeon to the Royal Infirmary, Glasgow. He volunteered for service in the South African war, and was senior medical officer to the Ladysmith, Pinetown, and Merebank camps. In 1903 he settled in general practice at Llangefni, where he remained for the rest of his life. During the first world war he held a commission in the R.A.M.C. and had charge of various auxiliary hospitals, as he also had during the last war. He was medical officer to the County Isolation Hospital for many years. An accomplished horseman for over fifty years, he was one of the most active members of the Anglesey Harriers. He married Miss Grace Rowlands, of Clegir Mawr, Anglesey, and she, with their three daughters, survives him.

Professor O. HERBERT WILLIAMS writes: Dr. Griffith Llewelyn Jones was the perfect family doctor. He had a keen and lively intelligence, unbounded energy, an understanding mind, and an inexhaustible fund of kindness, which he lavished on his patients. His response to a medical call was immediate. He used to dart along the Anglesey lanes like a swallow to see his patients, and he accomplished a prodigious amount of work in the 24 hours, but once inside the sick-room he was never in a hurry. He had that skill, which is tending to disappear, of making a remarkably accurate assessment of the patient's condition from symptoms and physical signs and with the aid of the simple armamentarium of the doctor's bag. Nevertheless, he was fully alive to the latest laboratory aids to diagnosis and made full use of them. If one of his patients was transferred to hospital or to a nursing-home he still kept in constant touch, for he considered that he was always in overall charge of the case, and kept himself continually informed of the patient's progress. No man served his generation better than did Llewelyn Jones, and no one was held in higher esteem. This was plainly shown by the mourning crowds from all parts of the island and beyond who lined the streets of Llangefni and congregated at the old church of Llangristiolus to pay their last homage to one who was indeed a "beloved physician."

Dr. N. H. Joy, who died at Chichester on January 20 at the age of 78, was the author of several well-known books on natural history. H. B. writes: Norman Humbert Joy was the son of a clever father and was himself of a rare type. As a student at St. Bartholomew's Hospital he was above the average at work and games, but his scope in both was curtailed by the need to qualify as quickly and inexpensively as possible. After a house-surgeoncy at the Southport Infirmary and a short assistantship in private practice, he became doctor to Bradfield College, an appointment for which he was well adapted. His domestic happiness and professional outlook were, however, early shattered by a motoring accident which left him a permanent cripple. Thereafter his energies were mainly confined to natural history, in which his powers of observation were extraordinary. He once said to me, "I know only part of my brain is working"; but in spite of this, and in spite of diplopia, severe headaches, and other handicaps, he had some notable achievements. He produced a large two-volume work on British beetles, illustrated by himself, which is still the standard book on the subject. He wrote also a small handbook on the identification of British birds in the field; this quickly went through several editions, and, like the beetle book, was illustrated by himself. During his lifetime he added more new species to the list of British beetles than anyone else; and once, while crossing Windsor Park, he discovered an ant new to science, named by Rothschild *laetitia* in a play on Joy's name. Among other exploits Joy made a complete collection of British butterflies, which he characteristically gave to a London museum. Another of his successful accomplishments which I like to remember was the photography of a cuckoo laying an egg. Through the 60 years of our friendship I have been continually inspired by Joy's brave mastery over cruel frustrations. He leaves two married daughters and a son who prospers as a doctor in the West Country. They have our sympathy with their sad memories.

We record with regret the death of Dr. E. E. PAGET-TOMLINSON at his home at Summerhill, near Ulverston, Lancashire, on January 20, at the age of 70. Edward Edmondson Paget-Tomlinson was born on April 26, 1882, the son of the late Dr. W. S. Paget-Tomlinson, of Kirkby Lonsdale. At Trinity Hall, Cambridge, he distinguished himself as an athlete, gaining a half-blue for the long jump. He also played Association football for the Corinthians, and was in a team which toured South Africa. From Cambridge he went on to the London Hospital, qualifying in 1909 and graduating M.B., B.Chir. in the following year. After holding house appointments at the London Hospital Dr. Paget-Tomlinson went into general practice in his home town of Kirkby Lonsdale, in Westmorland, and then moved to Malton, in Yorkshire, where he stayed until he entered the R.A.M.C. to serve in the war of 1914–18, much of the time in Salonika. He proceeded to the degree of M.D. in 1920 and then practised for some 15 years at Horncastle, Lincolnshire, where he was medical officer of health to the urban district council and honorary surgeon to the War Memorial Hospital and Dispensary. He left Horncastle early in 1935 and for a time lived at West Tanfield, near Ripon, and at Bedale, Yorkshire, until in 1938 he settled at Summerhill. For some years he had been in poor health, but during the last war he came out of retirement to help doctors in the Ulverston area. He was a governor of Sedbergh School and a magistrate on the Ulverston bench. He leaves a widow and one son.

We are indebted to Sir PHILIP MANSON-BAHR for the following appreciation: Dr. E. E. Paget-Tomlinson, or "P.-T." as he was known, was a friend and fellow student of mine at the London Hospital from 1905 to 1908. There are others of my contemporaries who will treasure the memory of "P.-T.'s" many lovable characteristics. He was the type of athletic student of his day, fresh from the University of Cambridge and excelling in every form of field athletics, especially in the jumps and hurdles. He was good to look upon, with his neat, well-proportioned figure and his charming, cheery smile. He was gifted with a particularly inquiring mind and would pose questions on all kinds of subjects, ending his inquiries always with a throaty chuckle. He was the most humble and modest of men, but under his diffidence there lurked a sincerity and a love of his fellow creatures. He was thus fitted with those qualities most needful to become a successful country practitioner. He filled the bill so well that his name has gone down as a household word in Lancashire and Lincolnshire, wherever he worked. He was a good naturalist and a keen observer of plant and bird life. It was always a pleasure to look forward to meeting him at reunion dinners of the London Hospital, but of recent years his visits became rare, and it is sad to think that such a fine, athletic person as "P.-T." should have suffered so much in his last long illness.

Dr. A. F. GOLDSMITH, who was for many years a greatly respected medical practitioner in Bedford, died on January 27 at the age of 82. Born at Bedford on June 18, 1870, the youngest son of the late Dr. G. P. Goldsmith, who had practised in the town for over 40 years, Arthur Frederick Goldsmith was educated at Bedford School and at St. George's Hospital, London, qualifying M.R.C.S., L.R.C.P. in 1894. Soon after qualification he joined his father and his brother, Dr. G. Harvey Goldsmith, who died in 1940, and he and his brother succeeded to the practice

when their father retired in 1904. Dr. A. F. Goldsmith himself retired in 1932 and for a time lived in Cornwall, but his home in recent years was at Biddenham, near Bedford.

Dr. H. DEAN POLLARD writes: As a contemporary colleague I would like to add a personal tribute to the late Dr. A. F. Goldsmith. I first met him when he had been in practice about three years, and we were often in contact since then. "Dr. Fred," as he was almost universally known, was a modest, unassuming, but greatly loved practitioner, one of the old school, who made friends of his patients but who did not make patients of his friends. His kindness and generosity to his poor patients were unstinted, but were known by them alone. He married, somewhat late in life, Miss Helen Rickard, a member of a well-known Bedford family, and he retired so that he could devote his whole attention to his wife, whose health was not robust. I cannot omit a reference to his zeal and enthusiasm for his church, St. Paul's, where he worked for many years in different offices, especially in connexion with the Sunday school. It irradiated his whole life and shone out in his geniality, his kindness, and his self-sacrificing hard work for poorer brethren.

Dr. WALTER SHARPIN writes: Fred Goldsmith was a contemporary of mine from my early student days at St. George's Hospital, and, although he was my senior by a year, he became one of my friends. He was known as a quiet, hard-working student and he gained the prize in anatomy for his year. When he gave up his practice in Bedford his patients felt his loss very keenly. Among his colleagues he was deservedly popular, being always cheerful, always loyal, a true friend, and one who had no enemies.

Dr. J. A. LEAHY writes: With the passing of Dr. A. F. Goldsmith, Bedford has lost a much-loved citizen and the medical profession a colleague who was held by all in terms of sincere affection and esteem. He was the last of a family of doctors, which included an ophthalmic surgeon, the late Dr. Harvey Goldsmith, who had practised in Bedford for nearly 70 years. It was my good fortune to succeed "Dr. Fred" in practice, but it was difficult to follow in the footsteps of a man whose kindness, cheerfulness, wit, and good humour were a by-word in Bedford; even a passing acquaintanceship showed him to be "full of the milk of human kindness." His old patients still talk of his skill and of his never-failing generosity, especially to the poor; and he possessed in ample measure the greatest of all virtues, Christian charity. His deep religious faith, manifest to all, enabled him to bear with Christian fortitude the infirmities which afflicted him towards the end of his days. He is buried in his beloved Biddenham close to the south wall of the church where he worshipped.

Dr. LESLIE LYNE, whose sudden and untimely death at the age of 57 occurred on February 2, was born on April 21, 1895, and educated at St. Olave's Grammar School and Guy's Hospital. As a result of this early and long association he acquired an affection for "The Borough" and its inhabitants which neither time nor separation could dull. After qualifying in 1919 Dr. Lyne held the posts of house-physician to Dr. (later Sir) Arthur Hurst and obstetric resident at Guy's. Subsequently he widened his experience by spending two years in India and Persia with the Indian Medical Service and a period as resident at Lambeth Infirmary before settling at Ascot at the suggestion of Sir Arthur Hurst. There he combined general practice with anaesthetics, being at one time on the staff of the King Edward VII Hospital, Windsor. But his real life's work began when, mainly for reasons of health, he moved to Hove in 1934. There his sterling qualities as a man and as a physician were quickly recognized and he soon formed a large and ever-widening circle of patients, who found in him the ideal family doctor—selfless, reliable, capable, and gentle. By them he will be greatly missed, perhaps not least by the aged, whose problems he seemed to understand so well. But in addition to the ties of a busy general practice he continued his interest in anaesthetics and held various appointments, most notably at the Sussex Throat and Ear Hospital, where he was senior anaesthetist for the past 14 years. Throughout innumerable operating sessions his quiet efficiency would allay anxieties and his unvarying good temper and charm alleviate tedium. Apart from his work, his happy family life occupied him entirely, and his joy was complete when in the same month last year his daughter graduated B.Sc. and his son M.B., B.Chir. To them and to his widow our deepest sympathy goes out in their irreparable loss.—T. S. A.

Dr. BERTRAM ROGERS, who died at Oxford on February 9 at the age of 92, spent most of his active professional life in Bristol. His father was J. E. Thorold Rogers, M.P., professor of political economy in the University of Oxford and at King's College, London. Bertram Mitford Heron Rogers was born on August 25, 1860, and was educated at Westminster School and at Exeter College, Oxford, where he gained a blue for Association football. He played at centre-half for the University against Clapham Rovers in the F.A. Cup Final at Kennington Oval in 1880. After leaving Oxford he began the study of medicine at University College, London, graduating B.M., B.Ch. in 1889 and proceeding M.D. in 1892. On going to Bristol he engaged in general practice, but was appointed physician to the Bristol Royal Hospital for Sick Children and Women, and more or less specialized in children's diseases at a time when that was very unusual, at any rate in the provinces. At the Annual Meeting of the B.M.A. in 1894 he was one of the secretaries of the Section of Diseases of Children and vice-president of the Section at the Annual Meeting in 1902. A member of the Territorial Army, he commanded a field ambulance in the war of 1914–18, and attained the rank of lieutenant-colonel. He was very active in local affairs, being president of the Bristol Medico-Chirurgical Society in 1910 and editorial secretary to its journal. He was local secretary of the British Association twice, in 1898 and 1930, chairman of the Bristol branch of the St. John Ambulance Association, and honorary treasurer of the local Royal Empire Society. As may be gathered from this record, he was highly esteemed by his colleagues, but few of them, if any, are left now to mourn his loss. After his retirement from clinical practice he worked for a time as a regional medical officer of the Ministry of Health. He married Agnes Fletcher in 1891, and had two daughters. Mrs. Rogers died in 1939.

Medical Notes in Parliament

Antibiotics for Fattening Stock

The Therapeutic Substances (Prevention of Misuse) Bill occupied the House of Lords for only a short time on its second reading on February 12.

The EARL OF ONSLOW, moving it, said that no one quarrelled with the Penicillin Act, 1947, but other substances had since come forward, and this Bill sought to regulate them so that their use should not be detrimental to the public. This applied particularly to isoniazid, which was cheap to produce, and could, if used for self-medication or without proper advice, do a great deal of harm to the person concerned. The other main purpose of the Bill was to permit the use of some of these drugs, particularly at the moment penicillin, in the feeding of pigs and table poultry. A tiny quantity of penicillin in their diet fattened them more quickly, and thus produced more pork and bacon.

The only substantial point raised in the discussion was put most succinctly by Lord O'HAGAN, although other peers spoke about it. It was to seek assurance that the effect of the inoculation of pigs by penicillin would neither be

deleterious to human beings who were allergic to penicillin when the pig-meat was eaten, nor conversely affect the effectiveness of the drug when it was properly administered to human beings.

The EARL OF ONSLOW assured them that the Agricultural Research Council and the Medical Research Council were satisfied that penicillin fed to pigs in this form could do no harm whatever.

As a footnote to this debate, an answer given in the House of Commons on February 12 stated that the Minister of Health was advised that the quantities of antibiotics needed would be minute—of the order of 2 to 20 parts in a million—and that there would remain in the meat from stock so fattened no traces of a kind that would entail any risk to the consumer.

Chemicals in Food

Mr. D. W. WADE asked the Minister of Food on February 11 what investigations he was undertaking into the use of chemicals and synthetic substitutes in the production of food, and when he would be able to publish the results.

Major G. LLOYD GEORGE replied that the Food Ministry did not itself undertake investigations of this nature. The work was carried out through continued consultation with the Health Departments and the Medical Research Council and by close co-operation with the Industrial Research Associations and other technical bodies concerned.

Mr. WADE said there had been an alarming increase in recent years in the use of chemicals in the production and processing of food, and there had been no adequate inquiry into either the short-term or long-term effects on the health of the nation.

Major LLOYD GEORGE would not accept the phrase "alarming increase." Chemicals need not necessarily be a cause for alarm; they had been used for many years in foodstuffs. Very careful investigation indeed was going on into important aspects of the matter.

Treatment of Flour

The MINISTER OF FOOD, answering a question by Mr. R. BELL on February 11 asking why, and under what authority, chalk is added to the national loaf, stated that calcium carbonate was added to National flour to ensure that total food supplies provided sufficient calcium to meet nutritional requirements. This was done under Articles 2 and 6 of the Flour Order, 1952, and Article 2 of the Bread Order, 1952. The addition of nutrients to flour was under discussion with the trades concerned, and an announcement would be made when the details had been settled.

Mr. D. W. WADE asked the Minister what progress had been made in the investigations into the existing methods of treatment of flour, and whether he would give an assurance that the process of agenization would be abandoned. Major G. LLOYD GEORGE stated that these complex and important investigations into possible alternatives to agene as a flour improver were requiring considerably more time than was originally thought necessary. They were being pursued with all possible speed, but it would be premature to take any action until they were completed.

In a further reply he said that since the investigations started one or two possible alternatives had been suggested, but it was obvious that careful research must be undertaken before either could be accepted.

Mr. G. NICHOLSON asked whether it had been accepted that agene was a contributory factor to hysteria in dogs.

Major LLOYD GEORGE said that was one of the things the committee was investigating. He also pointed out that agene had been used in bread in this country for over 30 years.

Lung Cancer

Mr. S. T. SWINGLER asked the Parliamentary Secretary to the Ministry of Works, as representing the Lord President of the Council, for a statement on the lines of research into the incidence of lung cancer among gas workers to be pursued by the Medical Research Council.

Mr. A. H. E. MOLSON replied on February 10 that the possibility of conducting further research on the incidence of lung cancer among gas workers was still under discussion by the Medical Research Council in consultation with other departments. He was therefore unable to make any statement at present about investigations which might be undertaken in the future.

London Sickness Claims

Lieutenant-Colonel M. LIPTON asked the Minister of National Insurance to what extent the number of claims for sickness benefit in the London area during December, 1952, exceeded the corresponding figure for 1951. Mr. O. PEAKE stated that the number of new claims to sickness benefit received in the offices of the Inner London region of the Department during the period of four weeks ending January 1, 1952, and December 30, 1952, were 52,770 and 77,040 respectively.

Lieutenant-Colonel LIPTON said that in view of this further evidence of loss caused by fog in London there should be more energetic action to deal with air pollution.

Elastic Stocking Prescriptions

Mr. W. W. HAMILTON asked the Minister of Health how many pairs of elastic stockings were supplied through the National Health Service on the prescription of general practitioners in the six months June–November, 1952; and what were the corresponding figures for each year since the inception of the Service.

Mr. IAIN MACLEOD, in a reply on February 6, said he regretted that when he answered a previous question on December 18 he omitted to make it clear that the figures he gave were for the hospital service only. Precise figures were not available, but it was estimated that the number of orders for elastic hosiery supplied on the prescription of general medical practitioners was at least ten times the number supplied through the hospital service. In his reply in December the Minister stated that the numbers supplied in June–November, 1952, were 16,055; in July–December, 1948, 4,788; and in the following complete years 23,331 (1949); 31,155 (1950); and 35,732 (1951).

Health Service Charges

Mr. A. BLENKINSOP asked the Minister of Health on February 12 what financial saving he estimated would result from the charges imposed under the Health Service Act, 1952, how much of this saving resulted from a fall in use of the services concerned, and how the savings compared with the estimates originally given. Mr. IAIN MACLEOD replied that the estimated amount of the charges paid or to be paid in 1952–3 by patients in England and Wales under the 1952 Act was about £2m. In addition, while figures to enable a complete estimate to be made were not available, the reduction in the demand for dental treatment and for hospital appliances for which charges were made compared with the previous year was estimated to show a saving of about £1,750,000. Comparisons could not usefully be made with estimates framed in the expectation that the charges would operate for a full year and before modifications in the original proposals were made.

Licence Duty on Cars

Lieutenant-Colonel W. H. BROMLEY-DAVENPORT asked the Chancellor of the Exchequer whether he was aware that, although veterinary surgeons, doctors, dentists, and midwives had been exempted under the Road and Rail Traffic Act (Exemptions) Regulations, 1951, from the necessity of obtaining a carrier's licence for their utility vehicles when used for carrying medicines, drugs, and instruments for use in their professional work, these vehicles were still subjected to the higher rate of Road Fund duty irrespective of ownership and use; and whether, in view of the difficulty for such

persons in obtaining small low-taxed private cars in substitution, he would take steps to ensure that the utility vehicles in question qualified for private-vehicle taxation rates.

Mr. J. A. BOYD-CARPENTER, the Financial Secretary, answered on February 12 that under section 5 of the Vehicles (Excise) Act, 1949, and s. 7 of the Finance Act, 1952, vehicles constructed or adapted for the conveyance of goods must pay duty as goods vehicles if used to convey goods for hire or reward or in connexion with a trade or business. He had no power to exempt particular classes from the general law.

Consultants in West Scotland

Sir THOMAS MOORE stated in a question to the Secretary of State for Scotland on February 10 that there was public concern in Ayrshire about the efficiency of the National Health Service and the shortage of trained medical and surgical consultants. Mr. J. STUART undertook to consider any particulars of deficiencies brought to his notice. Sir T. MOORE mentioned that there had been a disturbing number of resignations lately, especially among consultants. Mr. STUART said he was assured that the regional board were taking proper steps to replace those who had resigned. Mr. A. C. MANUEL said that doctors generally in West Scotland had expressed to him their satisfaction at the better service available since the National Health Service was begun.

Medico-Legal

LIABILITY OF HOSPITAL AUTHORITY

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

In an action for negligence against the surgical registrar of the Mayday Hospital, Thornton Heath, and the Croydon Hospital Group Management Committee in respect of the death of a patient from peritonitis after appendicectomy, a novel defence was raised on behalf of the management committee. The committee pleaded that in undertaking the care and treatment of patients they did so in pursuance of their duty to provide hospital specialist and general medical services under the National Health Service Act, 1946, that the surgical registrar was acting on their behalf in fulfilment of that duty, and that section 72 of the Act therefore relieved them of liability.

s. 72 of the Act of 1946 provides that s. 265 of the Public Health Act of 1875 shall have effect as if the authorities mentioned in it include hospital management committees. s. 265 of the Act of 1875 provides that no matter or thing done by local authorities shall, if done bona fide for the purpose of executing the Act, subject them personally to any action, liability, claim, or demand whatsoever.

But s. 13 of the National Health Service Act, 1946, provides that hospital management committees shall, notwithstanding that they may be exercising functions on behalf of the regional hospital board, be liable in respect of any liabilities incurred in the exercise of those functions, including liabilities in tort—for instance, for negligence.

This defence of the committee was tried as a preliminary issue in the action before Mr. Justice Parker on February 12.[1] In his judgment he said that it would be a very strange result if, in face of the plain words of s. 13 of the 1946 Act, the effect of s. 72 of that Act and s. 265 of the Public Health Act, 1875, absolved the committee from liability. It had been held in Scotland in *Davis* v. *Board of Management for Glasgow Victoria Hospitals*,[2] that, by reason of equivalent but not identical provisions in the statutes applicable to Scotland, the management committee could not be sued. But the decision was not binding on the English courts and Mr. Justice Parker felt unable to follow it. He decided the preliminary issue against the management committee, but granted leave to appeal.

This is apparently the first time in England since the National Health Service Act, 1946, came into force that a hospital management committee has relied on this defence. Lawyers and management committees throughout the country will await with great interest the result of an appeal from Mr. Justice Parker's decision, which is of the highest medico-legal importance.

[1] *The Times*, February 13.
[2] 1950, S.C. 382.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on January 22 the degree of D.M. was conferred on T. Stapleton and F. J. Flint.

The following reappointments are announced: A. G. McD. Weddell, M.D., Reader in Human Anatomy, from October 1, 1953, to September 30, 1960; and D. C. Sinclair, M.D., Demonstrator in Human Anatomy, and George Gordon, D.M., Demonstrator in Physiology, both from October 1, 1953, to September 30, 1958.

Among the honorary degrees the University proposes to confer at a Convocation on July 1, in connexion with the Rhodes Centenary, is that of D.C.L. on Professor W. G. Penfield, F.R.S., who was awarded the Order of Merit in this year's New Year Honours.

UNIVERSITY OF CAMBRIDGE

The establishment of the Elisabeth Storey Fund for research on leukaemia and allied diseases was announced in the *Journal* of December 6, 1952 (p. 1267). The Vice-Chancellor of the University announced on January 12 that he had received a gift of £220 from Mtre Mahmoud El-Darwish for use in connexion with the fund.

Professor J. S. Mitchell, F.R.S., has been appointed representative of the University at the seventh International Congress of Radiology, to be held at Copenhagen in July.

In Congregation on December 23, 1952, the following medical degrees were conferred by proxy:

M.B., B.CHIR.—J. M. S. Grieve, H. E. Lichtenstein, T. M. O. Morris, R. D. W. Romanis, H. C. M. Walton, M. H. Bennett, R. Ll. Morgan, J. F. Preece, T. L. Ringrose, J. O. Winter, M. D. Heyman, P. M. H. Rack, I. F. Smith, G. D. Stones, P. A. Watt, W. M. Beatley, W. A. G. Roper, M. C. Thornton, D. A. P. Burton, A. M. B. Golding, B. S. Jay, P. L. Maybury, K. F. Morrice, F. Reiseger, C. S. Savage, L. J. Stretton, I. Weinbren, R. K. Greenwood, H. F. Grundy, I. S. Lister, M. T. O'Donnell, I. A. Stewart, D. S. Trouton, R. C. Curry, S. H. Dallas, B. L. Hoskyns, H. S. Chen, E. M. Orton, J. T. H. Pick, J. A. M. Tudor-Hart, A. E. Wagstaff, D. W. K. Bird, W. H. Chapman, S. J. Fisher, D. B. Fox, E. P. Simkin, A. W. Warltier, F. L. Whalley, C. W. M. Adams, L. P. Balfour-Lynn, A. N. Griffith, R. D. Hernaman-Johnson, T. L. Scully, J. A. Fiddian, W. G. Williams, Aileen B. Donnison, Ruth M. Turner, Mrs. Hanna French, Vera M. C. B. P. Hollyhock, Gillian G. Matthews, G. M. P. Boyes.

The Council of the Senate of the University has accepted the offer of a grant by the Nuffield Foundation of £8,650 spread over five years in support of work in experimental embryology under the direction of Professor J. D. Boyd in the Department of Anatomy, and an additional grant from the Foundation of £550 a year for the three years of the grant for work on cellular biology to be conducted under the direction of Professor David Keilin, F.R.S., in the Molteno Institute of Biology and Parasitology (see also *British Medical Journal*, November 15, 1952, p. 1106).

In Congregation on February 6 the following medical degrees were conferred:

M.D.—I. S. Hodgson-Jones.
M.B., B.CHIR.—I. M. Brown (by proxy).

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on February 12, with Sir Cecil Wakeley, President, in the chair, the death of Sir Holburt Waring (Past President) was reported and the Council unanimously adopted a resolution of condolence.

An Honorary Fellowship was awarded to Professor Reynaldo dos Santos, of Lisbon.

Mr. Geoffrey Keynes was presented with the Cecil Joll Prize.

A Hunterian Lectureship was awarded to Professor Wilder Penfield, O.M., Hon.F.R.C.S., of Montreal, and a Moynihan Lectureship to Dr. H. L. Jaffe, of New York.

The Hallett Prize was awarded to Dr. A. T. Matheson (Capetown) and the Handcock Prize to Mr. A. H. Tooley (King's College Hospital).

It was reported that gifts had been received from Lord Webb-Johnson (bringing his total contribution to the Restoration and Development Fund to £2,500), from Professor A. V. Neale, and from Professor A. J. E. Cave.

Diplomas of Membership were granted to J. R. B. Saxby and to the recipients of the diploma of L.R.C.P. printed in the *Journal* of February 7 (p. 342).

Diplomas in Public Health, in Industrial Health, and in Anaesthetics were granted, jointly with the Royal College of Physicians of London, to the candidates whose names were printed in the report of the meeting of the Royal College of Physicians of London in the *Journal* of February 7 (p. 342).

Hospitals were recognized under paragraph 23 of the F.R.C.S. regulations as follows: North Middlesex Hospital, Edmonton, *decennial revision*, three surgical registrars, for a year; six house-surgeons, for six months. Warneford General Hospital, Leamington Spa, *decennial revision*, resident surgical officer; house-surgeon, both for six months; *from January, 1954*, casualty officer. Royal Victoria Hospital, Folkestone, *decennial revision*, resident surgical house-surgeon (until February, 1954), for six months. Lewisham Hospital, *paragraph 23c*, ear, nose, and throat registrar. Central Middlesex Hospital, *paragraph 23c*, ear, nose, and throat registrar. County Infirmary, Louth, resident surgical officer, for six months. Fulham Hospital, *additional recognition*, orthopaedic house-surgeon, for six months. Southmead Hospital, Bristol, *additional recognition*, house-surgeon (genito-urinary), for six months; *from January, 1954*, two casualty house officers. Royal East Sussex Hospital, Hastings, *from January, 1954*, casualty officer. West Norfolk and King's Lynn General Hospital, *from January, 1954*, casualty officer. Maidenhead Hospital, *from January, 1954*, casualty officer. Dreadnought Seamen's Hospital, London, *from January, 1954*, casualty and receiving-room officer. Ingham Infirmary, South Shields, *from January, 1954*, casualty officer. Chelmsford and Essex Hospital, *from January, 1954*, casualty officer. Wanstead Hospital, *from January, 1954*, casualty officer: King George Hospital, Ilford, *from January, 1954*, casualty officer. West Middlesex Hospital, *from January, 1954*, two senior house-surgeons (casualty department). Rochdale Infirmary, *from January, 1954*, resident casualty officer. Selly Oak Hospital, Birmingham, *from January, 1954*, two casualty officers (senior house officers). Worcester Royal Infirmary, *from January, 1954*, casualty officer (senior house officer). Walsall General Hospital, *from January, 1954*, casualty officer.

ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH

At a quarterly meeting of the College held on February 3, with the President, Dr. W. A. Alexander, in the chair, the following were elected Members of the College: D. G. McIntosh, D. G. C. Whyte, M. P. Goel, L. S. C. Mendis, G. M. Baird, B. Bevan, D. P. Gupta, J. B. Gibson, A. D. Muldoon, F. C. Friedlander, L. Rabinowitz, S. A. Syed, W. Frain-Bell, J. Paul, C. Marks, C. H. Sivaraman, E. M. McLachlan, J. M. Neilson, R. H. Gosling, A. R. Somner, S. J. Cohen, D. H. H. Pullon, M. Dan, Z. H. El Massry, S. Sing, J. A. Chunn, J. L. Potter, S. J. Irani, P. Sobti.

The Services

The *London Gazette* has announced the creation of the rank of Surgeon Rear-Admiral (Dental) with effect from October 1, 1952. The announcement states that the Lord Commissioners of the Admiralty are of the opinion that the duties of the Senior Dental Officer have so increased in scope as to justify the new rank.

Surgeon Lieutenant J. I. McL. Forsyth, R.N.Z.N. (*H.M.N.Z.S. Taupo*), and Temporary Surgeon Lieutenant R. A. Rowan, R.N.V.R. (*H.M.S. Belfast*), have been mentioned in dispatches for distinguished service in operations in Korean waters.

Major A. B. Kerr, O.B.E., T.D., R.A.M.C., has been awarded the First and Second Clasps to the Territorial Efficiency Decoration.

The Air Ministry has announced the upgrading of the post of Director of R.A.F. Dental Services, which is now to be held by an officer of the R.A.F. dental branch in the rank of Air Vice-Marshal.

Vital Statistics

Influenza

In the week ending February 7 there were 446 deaths from influenza in the great towns of England and Wales. In the previous week there were 313. Since the beginning of the year there have been 1,014 deaths in the great towns as compared with 197 in 1952 and 5,914 in 1951. The increased mortality in the week reviewed was mainly confined to London and the south-eastern region, where the deaths were 123 more than in the preceding week. The deaths in the towns of the eastern region were 22 more and in the southern region 17 more; in the remainder of the country the deaths were only 19 more than in the preceding week.

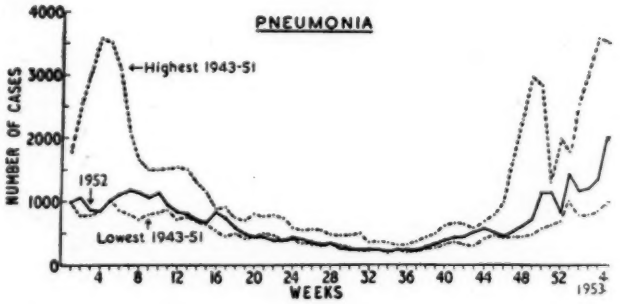
Although virus B has occasionally been demonstrated, the organism mainly responsible is a virus A-prime closely related to the Scandinavian type. Probably the serological type of the virus does not in general determine the severity of the disease except in so far as it is an antigenic novelty in a community without any resistance to it.

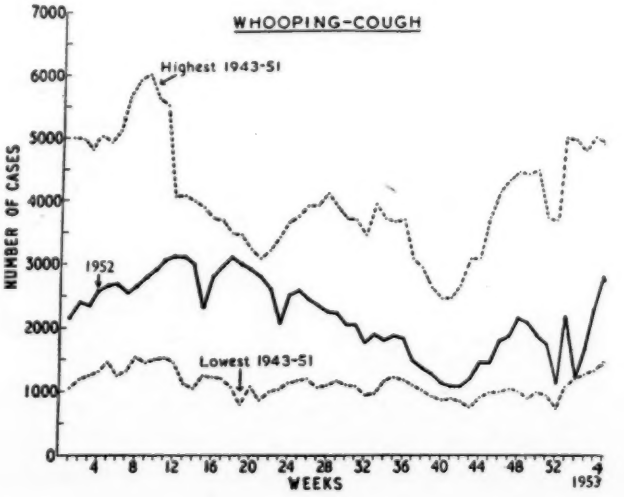
Week Ending February 7

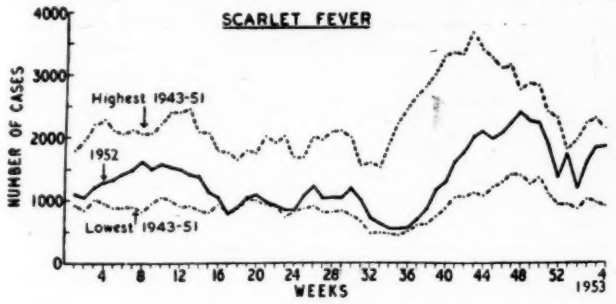
The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,545, whooping-cough 2,571, diphtheria 16, measles 31,494, acute poliomyelitis 26, dysentery 286, paratyphoid fever 15, and typhoid fever 2.

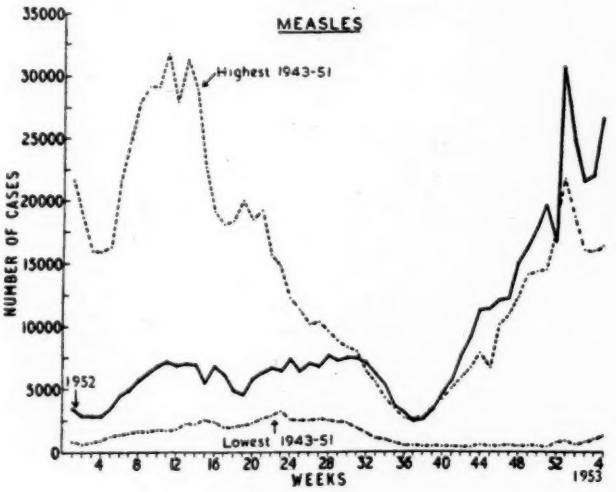
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1943–51 are shown thus - - - - - - - -, the figures for 1952–3 thus ————. Except for the curves showing notifications in 1952–3, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

With the exceptions of a rise of 4,578 in the number of notifications of measles, from 21,882 to 26,460, and 680 for acute pneumonia, from 1,349 to 2,029, only quite small variations were reported in the incidence of infectious diseases in England and Wales during the week ending January 31.

The largest increases in the number of notifications of measles were 607 in Yorkshire West Riding, from 1,182 to 1,789; 514 in Middlesex, from 1,574 to 2,088; 422 in Devonshire, from 314 to 736; 316 in Lancashire, from 1,843 to 2,159; 250 in Sussex, from 516 to 766; 241 in Durham, from 587 to 828; 223 in Surrey, from 685 to 908; 203 in Staffordshire, from 663 to 866; and 202 in Warwickshire, from 1,184 to 1,386. Only small variations occurred in the local trends of scarlet fever and whooping-cough. The number of notifications of scarlet fever was 1,850, 18 more than in the preceding week, and the notifications of whooping-cough, 2,799, were 7 more than in the preceding week. 24 cases of diphtheria were notified—an increase of 5 on the preceding week. Half of the cases were notified in two counties, Lancashire 5 (Liverpool C.B. 4) and Warwickshire 7 (Birmingham C.B. 7). The notifications of acute pneumonia were the highest for almost two years. The largest rises during the week were 74 in Middlesex, from 97 to 171, and 68 in Yorkshire West Riding, from 128 to 196.

29 cases of acute poliomyelitis were notified during the week—7 more for paralytic cases and 2 fewer for non-paralytic cases than in the previous week. The largest returns were 3 in each of the counties of Berkshire, Essex, Lancashire, and London.

The 435 notifications of dysentery were 16 more than in the preceding week. The largest returns were Lancashire 116 (Liverpool C.B. 52, Warrington R.D. 24, Salford C.B. 10), Essex 91 (East Ham C.B. 89), Lincolnshire 40 (Grimsby C.B. 38), London 32 (St. Pancras 9), Yorkshire West Riding 31 (Leeds C.B. 13), Cambridge 23 (Cambridge M.B. 23), Middlesex 17 (Edmonton M.B. 7), and Kent 16 (Penge U.D. 10).

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **January 31** (No. 4) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	24	1	9	1	0	27	1	14	1	2
Dysentery	435	32	110	6	0	547	38	72	2	
Encephalitis, acute	8	2	0	0		6	0	1	0	
Enteric fever: Typhoid	1	0	0	0	7	2	0	0	0	0
Paratyphoid	7	0	2(B)	0	0	10	2	1(B)	0	
Food-poisoning	60	6		1		90	8		0	
Infective enteritis or diarrhoea under 2 years				13	12				10	9
Measles*	26,460	1470	273	49	178	2,837	41	287	143	61
Meningococcal infection	45	5	12	0	2	37	3	11	1	2
Ophthalmia neonatorum	32	2	5	0		30	4	9	0	
Pneumonia†	2,029	183	245	61	25	836	38	294	10	1
Poliomyelitis, acute: Paralytic	22	2	1	0	4	18	0	1	0	2
Non-paralytic	7	1				9	0			
Puerperal fever§	282	32	16	0		207	28	14	1	2
Scarlet fever	1,850	85	292	41	57	1,293	39	233	36	34
Tuberculosis: Respiratory			165	27				154	37	
Non-respiratory			21	4				19	8	
Whooping-cough	2,799	153	159	35	187	2,573	86	318	152	75

DEATHS in Great Towns	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	1	0	0		0	0	0		0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0		0	
Infective enteritis or diarrhoea under 2 years	11	2	3	1	1	13		4	0	1
Influenza	313	54	2	2	5	33	4		2	0
Measles		0	1	0	0		0		0	0
Meningococcal infection		0	1				1			
Pneumonia	654	153	29	15	11	303	41		7	8
Poliomyelitis, acute	4	0			0	0	0			0
Scarlet fever		0	0	0	0		0		0	0
Tuberculosis: Respiratory	145	28	20	2	7	176	26	30	2	13
Non-respiratory		5	3	1	1		4	3	1	0
Whooping-cough	4	0	1	0	0	1	0		0	0
Deaths 0–1 year	321	37	38	13	14	269	31	30	14	24
Deaths (excluding stillbirths)	8,403	1542	621	143	189	6,345	964	754	135	202
LIVE BIRTHS	7,437	1103	849	228	419	7,564	1164	840	217	413
STILLBIRTHS	211	27	27			194	15	31		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Hunterian Society.—The annual dinner of the Hunterian Society was held at the Savoy Hotel on February 12, when the president, Dr. B. Parsons-Smith, was in the chair. Lord Reading, in proposing the health of the Society, referred to its "long and fluctuating" history and its close connexion with the City of London. "To doctors patients are a virtue, and to some patients doctors are a vice," was one of his witty remarks. In response the president gave an account of the Society's activities in the past year. The Lord Mayor, Sir Rupert de la Bere, was welcomed in a gracious speech by Mr. J. H. Doggart. The Lord Mayor, in reply, mentioned the intensive voluntary work at the Mansion House for the flood relief fund. The toast, "The guests and kindred societies," was proposed by Dr. George Day in a witty speech which kept everyone anxiously guessing what he might say next. Sir Raymond Evershed and Dr. F. M. R. Walshe replied.

Pharmacy Bill.—The removal of the disqualification upon members of the medical profession from being registered as pharmaceutical chemists is one of the objects of the recently published Pharmacy Bill. The Bill is a private Member's Bill with support from both sides of the House. Other provisions include the creation of a single statutory register of pharmacists and the extension of the powers of the Pharmaceutical Society in connexion with the examination and registration of pharmacists.

R.S.I. Prize Essays.—The Royal Sanitary Institute is offering two open prizes this year for essays on health subjects. The prizes are the John Edward Prize of £60 for an essay on "Internal planning lay-out and equipment of dwellings to reduce domestic work without loss of efficiency and within reasonable expenditure"; and the John S. Owens Prize of £15 for an essay on "The location of industry having regard to the health of the people." Intending competitors should apply to the secretary, The Royal Sanitary Institute, 90, Buckingham Palace Road, London, S.W.1, for a copy of the conditions. The last date for entries is December 31.

Family Doctor.—In the March issue of *Family Doctor* Professor W. C. W. Nixon and his colleagues complete their series of articles on having a baby. To judge from the two pages of correspondence on the propriety or otherwise of dealing openly with this subject in a family magazine, readers have been both interested and helped. In the same issue, Dr. T. Anderson summarizes the arguments for and against whooping-cough immunization. On psychological questions there are articles by Miss Alcock on the "schoolgirl crush" and by Professor R. S. Illingworth on "family favourites." Articles of general interest include accounts of what is being done for spastics and old people, and the story of a seven-months voyage in a whaler.

New Cancer Periodical.—The first volume of *Advances in Cancer Research* has just been published by the Academic Press, New York. It is edited by Professor Alexander Haddow (Royal Cancer Hospital, London) and Dr. J. P. Greenstein (National Cancer Institute, Bethesda, Md), and is designed to present authoritative reviews on various phases of cancer research. It is international in scope; vol. 1 (590 pages) is priced at $12.00 (£4 6s.).

Extension of Bart's.—The Court of Common Council has approved plans for the building of a 120-bed extension to St. Bartholomew's Hospital, London. The site for the new block is separated from the main hospital buildings by a street, and a tunnel will be needed to link the two together. It is not yet known when building will be begun.

Coccidiodin, Histoplasmin, and Blastomycosis Antigen for diagnostic skin tests are now obtainable from the department of pathology, St. John's Hospital for Diseases of the Skin, Lisle Street, London, W.C.2 (Tel. Gerrard 8383, Ext. 22), instead of from the London School of Hygiene and Tropical Medicine as previously.

Colyer Prize.—The Royal Society of Medicine invites applications for the triennial Colyer Prize for the best original work in dental science during the preceding five years. The prize is valued at £20. The closing date for applications is September 21.

Refresher Course Book.—Copies of the first Refresher Course book are now available once more. The first impression, which appeared last October, sold out shortly after publication. The book contains all the Refresher Course articles printed in the *Journal* from October, 1949, to December, 1950. Each article has been revised by its author and brought up to date. Copies of the book may be obtained from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1. The price is 25s.

Emergency Bed Service: Applications and Admissions.—During the seven days ending February 16 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 1,730, of whom 77.93% were admitted. A yellow warning indicating that the percentage of admissions fell below 80 was issued on February 10.

Dr. L. Justin-Besançon, professor of medicine at the Sorbonne, has been elected a member of the French Academy of Medicine.

COMING EVENTS

Robert Campbell Memorial Oration.—Dr. E. E. Pochin will deliver a Robert Campbell Memorial Oration on February 26 at 8.30 p.m. in the Whitla Medical Institute, Belfast. His subject is "The Value of Radioactive Isotopes in Medicine."

Chesterfield Medal in Dermatology.—The examination for the Chesterfield Medal will be held on March 9, 10, 18, and 19. February 28 is the closing date for entries, which should be lodged with the secretary, Institute of Dermatology, Lisle Street, London, W.C.2.

Postgraduate Examination Courses.—Courses for candidates for the D.M.R.D. and D.M.R.T. (R.C.P.Lond. and R.C.S.Eng.), commencing in October, 1953, are being organized by the Faculty of Radiologists. Further information will be found in the advertisement columns.

NEW ISSUES

Archives of Disease in Childhood.—The next issue (Vol. 128, No. 137) will be available in a week's time. The contents include:

REMNANTS OF THE VITELLO-INTESTINAL DUCT. A CLINICAL ANALYSIS OF 88 CASES. John Aitken.
OVARIAN AGENESIS OR PTERYGIUM SYNDROME. Per Skjelbred.
CHONDRODYSTROPHY WITH ECTODERMAL DEFECTS. E. J. Gallagher, M. E. MacGregor, and M. Israelski.
TYPHOID OSTEITIS IN INFANCY. Harris Jackson, I. Kessel, S. N. Javett, and P. Kushlick.
A CASE OF OSTEOMYELITIS OF ALL THE SMALL BONES OF HANDS AND FEET. M. D. Baber.
ACCIDENTAL POISONING OF YOUNG CHILDREN. Douglas Swinscow.
THE SENSITIVITY TO ANTIBIOTICS OF STRAINS OF BACT. COLI ASSOCIATED WITH INFANTILE GASTRO-ENTERITIS. J. Smith and W. H. Galloway.
KILLED ANTITUBERCULOUS VACCINE AND HYALURONIDASE (D.V.). G. Salvioli.
OBSERVATIONS ON FOETAL HAEMOGLOBIN. C. Gardikas, D. G. Scott, and John F. Wilkinson.
TENSION PNEUMOTHORAX COMPLICATING STAPHYLOCOCCAL PNEUMONIA AND EMPYEMA THORACIS. DESCRIPTION OF A CASE. R. Spencer.
HAEMANGIOENDOTHELIOMA OF THE LIVER SIMULATING CONGENITAL HEART DISEASE IN AN INFANT. C. Blaxland Levick and J. Rubie.
THE INCIDENCE AND SIGNIFICANCE OF SYSTOLIC CARDIAC MURMURS IN INFANTS. W. C. Taylor.
IDIOPATHIC RENAL ACIDOSIS IN TWINS, WITH ALKALOSIS RESULTING FROM OVERDOSAGE OF CITRATE MIXTURE. John Rendle-Short.
TREATMENT OF THE SCHOENLEIN-HENOCH SYNDROME WITH ADRENOCORTICOTROPHIC HORMONE (A.C.T.H.) AND CORTISONE. A REPORT OF NINE CASES. J. N. Briggs and M. G. Philpott.
THE URINARY EXCRETION OF HISTAMINE IN CHILDREN. H. M. Adam and R. G. Mitchell.
PNEUMOPERITONEUM AS A DIAGNOSTIC PROCEDURE. J. Rubie.
THE ABSORPTION OF CHLORAMPHENICOL IN THE NEWBORN. Donough O'Brien.
TWO CASES OF CHRONIC POLYNEURITIS IN CHILDREN. J. S. Oldham.
DUPLICATION OF THE ILEUM. W. S. Killpack.

Issued quarterly; annual subscription £2 2s.; single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

Details in this column are necessarily brief. Further information and tickets where required (marked ●) should be obtained from the institution concerned.

Monday, February 23

HUNTERIAN SOCIETY.—At Mansion House, 8.30 p.m., Hunterian Oration by Mr. A. Dickson Wright: Quacks of John Hunter's Time.

INSTITUTE OF PSYCHIATRY.—5.30 p.m., Dr. E. Stengel: lecture-demonstration for postgraduates.

MEDICAL SOCIETY OF LONDON.—8.30 p.m., pathological meeting.

UNIVERSITY COLLEGE.—At Physiology Theatre, 4.45 p.m., public lecture by Professor Jean Roche (Collège de France, Paris): Comparative Biochemistry of Iodoproteins.

Tuesday, February 24

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. P. L. Mollison: Life-span of Red Cells.

CHADWICK TRUST.—At 26 Portland Place, W., 2.30 p.m., Dr. G. Decharneux (Liége): Industrial Medicine and Hygiene in Belgium.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. L. Forman: Skin Diseases Related to Cancer.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor J. Moroney: Colonic Replacement and Restoration of the Human Stomach.

WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Dr. Colin Edwards: Neurological demonstration.

Wednesday, February 25

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. A. Dudgeon: Virus Diseases.

INSTITUTE OF UROLOGY.—At St. Paul's Hospital, W.C., 4.30 for 5 p.m., Mr. J. G. Sandrey: Vesical Neoplasms.

ROYAL EYE HOSPITAL CLINICAL SOCIETY.—5.30 p.m., clinical meeting; 6 p.m., film by Miss J. M. Dollar and Miss M. Savory: Exenteration of the Orbit.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Dr. James Watson Lecture by Mr. A. G. Macgregor: Thyrotoxicosis: Its Diagnosis and Treatment by Modern Techniques.

YORKSHIRE SOCIETY OF ANAESTHETISTS.—At Leeds General Infirmary, 8 p.m., Dr. G. E. Hale Enderby: Reduction of Surgical Haemorrhage by Controlled Hypotension.

Thursday, February 26

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. A. H. T. Robb-Smith: Functional Significance of Connective Tissue.

GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY.—At Glasgow University Union, 7.30 p.m., B.M.A. Lecture by Professor Ian Aird: Modern Exercises in the Hunterian Discipline.

●INSTITUTE OF CHILD HEALTH.—5 p.m., Dr. G. Stewart Prince: Emotional Problems of Puberty.

LIVERPOOL MEDICAL INSTITUTION.—4.30 p.m., Sir Russell Brain: Neurology of the Cervical Spine.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Sir Clement Price Thomas: Carcinoma of the Lungs (with lantern slides).

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Arris and Gale Lecture by Mr. L. P. Le Quesne: Management of Water and Electrolyte Administration during the Post-operative Period.

ST. ANDREWS UNIVERSITY.—At Physiology Department, Dundee, 5 p.m., Professor G. A. H. Buttle: Chloramphenicol, Aureomycin, and Terramycin and the Resistance Developed to Them.

SOCIETY OF CHEMICAL INDUSTRY: MICROBIOLOGY AND FOOD GROUPS.—At Institution of Electrical Engineers, 6.15 p.m., papers by Dr. C. Cockburn, Dr. R. E. O. Williams, and Dr. Joan Taylor: Pathogenic Organisms in Food.

UNIVERSITY COLLEGE.—At Physiology Theatre, 4.45 p.m., public lecture by Professor V. B. Wigglesworth, F.R.S.: Chemical Aspects of Insect Physiology.

WHITLA MEDICAL INSTITUTE, Belfast.—8.30 p.m., Robert Campbell Memorial Oration by Dr. E. E. Pochin: Value of Radioactive Isotopes in Medicine.

Friday, February 27

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. D. I. Williams: Alopecia.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—4.30 p.m., Mr. N. Asherson: Mastoiditis.

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—7.30 p.m., Dr. Denys K. Ford: Arthritis of Genital Origin—Treatment with A.C.T.H.

ROYAL INSTITUTE OF PHILOSOPHY.—At University Hall, 14, Gordon Square, W.C., 5.15 p.m., Dr. J. Hartland-Swann, B.Litt., Ph.D.: Nature of Mind.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Chartres.—On February 8, 1953, at Churchill Hospital, Oxford, to Mary (formerly Gaudin), wife of John C. Chartres, B.M., B.Ch., D.T.M.&H., a sister for Roger—Diana Crispin.

Cross.—On February 5, 1953, at King's College Hospital, London, S.E., to Pamela (formerly Hufeland), wife of Dr. A. F. Cross, a daughter—Melanie Jane.

Duff.—On February 13, 1953, at the Yarborough Nursing Home, Southsea, Hants, to Audrey, wife of Dr. Derek R. Duff, a daughter.

Morrison.—On February 11, 1953, to Ina, M.B., Ch.B., D.Obst.R.C.O.G. (formerly Alexina Myles), wife of Dr. Leslie G. Morrison, 8, St. Catherine's Place, Edinburgh, a daughter.

Rigby.—On February 5, 1953, to Joan, wife of Dr. J. P. V. Rigby, of Huntsmoor Weir, Cowley, Middlesex, a daughter.

Wollner.—On February 8, 1953, at the Churchill Hospital, Oxford, to Sylvia Wollner, M.B., B.S. (formerly Colquhoun), wife of Leopold Wollner, M.B., B.S., a son—Mark Edward.

Wurm.—On February 10, 1953, at King's College Hospital, London, to Rhonda, wife of Roger Wurm, M.B., M.R.C.O.G., a son—Jeremy.

DEATHS

Balme.—On February 13, 1953, Harold Balme, O.B.E., M.D., F.R.C.S., D.P.H., of 64, Copers Cope Road, Beckenham, Kent, formerly of Shantung, China, aged 74.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Gastric 'Flu

Q.—*Is there such a thing as gastric 'flu?*

A.—Gastro-intestinal symptoms may occur as a complication of true virus influenza. There is, however, no evidence that outbreaks in which the symptoms are predominantly gastro-intestinal have anything whatever to do with influenza. A form of gastro-enteritis due to a filterable agent has been described and outbreaks of Sonne dysentery may also masquerade as "gastric 'flu." The term may be a useful label for practitioners to use, but it has no scientific basis, and its use in publications may lead to confusion.

Wheat Gluten in Sprue and Steatorrhoea

Q.—*Does the exclusion of wheat gluten from the diet of adults with sprue or idiopathic steatorrhoea have the same beneficial effect as in coeliac disease in children?*

A.—The effect of excluding wheat gluten from the diet in adult cases of sprue and idiopathic steatorrhoea is still under investigation. Some cases undoubtedly show improvement, but it is too early to say whether this method of treatment will prove generally effective. It does not seem likely that any form of treatment can bring about dramatic recovery in patients with many years' history of steatorrhoea and multiple deficiencies. Chronic deficiency of nutrients alone may cause irreversible structural changes which may prevent or delay complete recovery.

Aetiology of Chronic Bronchitis and Emphysema

Q.—*What aetiological factors are of importance in the development of chronic bronchitis and emphysema? Are outdoor workers, such as policemen, specially liable to the condition?*

A.—Factors of importance in the aetiology of chronic bronchitis and emphysema are climatic, environmental and occupational, constitutional and hereditary, and the effect of smoking. Chronic bronchitis is principally a disease of those temperate climates which are liable to spells of cold, damp, foggy weather. The environmental factor may be illustrated by the much greater frequency of bronchitis and emphysema in industrial areas, irrespective of occupation. Among occupations, those which expose the worker to dust (even apart from those dusts known to be specifically harmful) and to violent changes of temperature show a high incidence of chronic bronchitis. Heavy physical work out of doors in all weathers, such as that of navvies, is said to be a factor, though there is no evidence that outdoor occupation in itself is important. Smoking is undoubtedly important, and giving up this habit is nearly always beneficial to the chronic bronchitic. In addition to these external factors, hereditary constitution plays an important part. Many patients whose final condition is best described as chronic bronchitis and emphysema start as asthmatics and show the well-known family predisposition to allergic disorders; apart from this, chronic bronchitis itself often seems to run in families. Whether chronic nasal sinusitis should be regarded as causing chronic bronchitis, or simply as another manifestation of the same underlying abnormality of the entire respiratory mucosa, is a matter of controversy.

Treatment of Psoriasis

Q.—*Have there been any recent notable advances in the treatment of psoriasis?*

A.—The treatment of psoriasis has unfortunately not altered. Year after year new treatments are introduced and praised and, before long, discarded. Undecylenic acid is now recognized to be useless; cortisone and A.C.T.H. are only of doubtful value. Other current and widely advertised treatments with proprietary remedies will, one suspects, go the way of the rest before long. Dr. R. M. B. MacKenna's Refresher Course article (*British Medical Journal*, 1950, 2, 207) still remains a complete and up-to-date summary of treatment.

Brittle Nails

Q.—*What is the present informed opinion of the cause and treatment of brittle nails—that is, nails which crack and flake at the edge? One authority says it is connected with the general health, another says it is due to detergents and degreasers. It is a very common complaint among women.*

A.—Both authorities are correct. There is no single cause; disturbances of general and nervous health are common causes, but external agents may be responsible, and often both factors play a part. Among external factors excessive manicuring, the use of enamels with ethyl acetate or acetone to dissolve them, and the use of alkaline cuticle removers are important. The moderate use of enamels may, however, be protective, but they should not be frequently removed. The effect of detergents and degreasers can in part be warded off by protective barriers.

Soaking in warm water and the inunction of olive oil are recommended as local treatment, together with attention to the general health.

Pyocyanea Infections

Q.—*What antibiotics are effective against Pseudomonas pyocyanea?*

A.—*Ps. pyocyanea* is totally insensitive to penicillin. It is usually resistant enough to the newer antibiotics to preclude successful treatment with them, although terramycin tends to be rather more active against it than either aureomycin or chloramphenicol. Sensitivity to streptomycin varies, some strains being highly resistant and others quite sensitive. The only antibiotic to which this organism is regularly and highly sensitive is polymyxin.

Either streptomycin or polymyxin may be used (the former assuming that the strain has been shown to be sensitive) for both the common forms of treatment called for in connexion with *Ps. pyocyanea* infections—namely, intramuscular injection for urinary infections, and local application for superficial sepsis, as in burns. The main advantage of streptomycin at present is that it is more easily obtainable, of polymyxin that it is more effective, particularly for the second purpose named. Both drugs can cause toxic effects, streptomycin on the eighth nerve and polymyxin on the kidney, but neither need be given for a urinary infection in such doses or for such a length of time that such complications need be feared. The local application of polymyxin is harmless from this point of view, as is its intrathecal injection for the treatment of meningitis.

Road Accidents

Q.—*What is the best immediate treatment for a shocked patient after a road accident? Are heat and morphine still regarded as good treatment?*

A.—In itself, shock is a meaningless term. Shock after a road accident should be treated according to its cause. The ill effects of road accidents may be due to fright (most commonly), to blood loss, internal injury, fracture, or fat embolism. External application of heat is important only for the patient's comfort, or if the patient has been left out for a long time in cold weather without protection. He should be given warm fluids, such as tea. Morphine is generally most useful, particularly if there is pain: a note should always be left on the patient saying what dose has been given, since serious overdosage sometimes occurs. In the absence of serious complications, the state of stress, mental and physical, should be dealt with by making the patient comfortable and by assuring him that there is no serious complication. If it is not possible to give this assurance he should be sent to hospital and told that a more adequate examination will be made there. Should any more severe complication be present, this should be treated according to accepted first-aid principles and the patient transferred to hospital.

Enteric-coated Ferrous Sulphate

Q.—*Are enteric-coated ferrous sulphate tablets absorbed by the intestine? Coating has been recommended to limit symptoms of intolerance in pregnant women, but I understand that iron is absorbed only from the pyloric end of the stomach and the first half of the duodenum.*

A.—Iron is absorbed from the stomach and from the small intestine, chiefly the upper part, but there is evidence that absorption can occur from lower parts of the intestine. The usual enteric coating should ensure the liberation of the tablet's contents in the alkaline part of the duodenum, although certain proprietary forms of coating may liberate the contents after contact with fluid which is not alkaline. It may be expected, therefore, that ferrous sulphate can be absorbed from enteric-coated tablets, but positive proof of this should be easy to obtain by serial estimation of the blood haemoglobin. If a pregnant woman is intolerant of ferrous sulphate it might be worth using one of the other preparations, such as iron and ammonium citrate mixture or a colloidal iron preparation such as Liq. Ferri Dialysati *B.P.C.*

Toxaemia of Pregnancy

Q.—*What is the present view of the aetiology and pathology of the toxaemias of pregnancy?*

A.—This question is beyond the range of a concise reply because the aetiology and pathology of toxaemias of pregnancy remain to a large extent obscure. The present-day tendency, however, is to regard the basis of toxaemia of pregnancy as uterine and placental ischaemia, with possibly associated imbalance of the endocrine functions of the placenta, adrenal, and pituitary.

Books of "Any Questions?"

Q.—*Are copies of both the first and second books of "Any Questions?" still available?*

A.—No. The first book has sold out after a total printing of 10,000 copies, but copies of the second book, published in December, 1952, are still available. Copies of the second book may be obtained from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, for 7s. 6d. (postage 6d.). Please order now so as to ensure getting a copy.

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